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(57) Abstract

Aminoalkyl glucosamine phosphate compounds that are adjuvants and immunoeffectors are described and claimed. The compounds have a 2–deoxy–2–amino glucose in glycosidic linkage with an aminoalkyl (aglycon) group. Compounds are phosphorylated at the 4 or 6 carbon on the glucosamine ring and comprise three 3–alkanoyloxyalkanoyl residues. The compounds augment antibody production in immunized animals as well as stimulate cytokine production and activate macrophages. Methods for using the compounds as adjuvants and immunoeffectors are also disclosed.

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DESCRIPTION

AMINOALKYL GLUCOSAMINE PHOSPHATE COMPOUNDS AND THEIR USE AS ADJUVANTS AND IMMUNOEFFECTORS

Background of the Invention

Humoral immunity and cell-mediated immunity are the two major branches of the mammalian immune response. Humoral immunity involves the generation of antibodies to foreign antigens. Antibodies are produced by B-lymphocytes. Cell-mediated immunity involves the activation of T-lymphocytes which either act upon infected cells bearing foreign antigens or stimulate other cells to act upon infected cells. Both branches of the mammalian immune system are important in fighting disease. Humoral immunity is the major line of defense against bacterial pathogens. In the case of viral disease, the induction of cytotoxic T lymphocytes (CTLs) appears to be crucial for protective immunity. An effective vaccine stimulates both branches of the immune system to protect against disease.

Vaccines present foreign antigens from disease causing agents to a host so that the host can mount a protective immune response. Often vaccine antigens are killed or attenuated forms of the microbes which cause the disease. The presence of non-essential components and antigens in these killed or attenuated vaccines has encouraged considerable efforts to refine vaccine components including developing well-defined synthetic antigens using chemical and recombinant techniques. The refinement and simplification of microbial vaccines, however, has led to a concomitant loss in potency. Low-molecular weight synthetic antigens, though devoid of potentially harmful contaminants, are themselves not very immunogenic. These observations have led investigators to add adjuvants to vaccine compositions to potentiate the activity of the refined vaccine components.

Presently, the only adjuvant licensed for human use in the United States is alum, a group of aluminum salts (e.g., aluminum hydroxide, aluminum phosphate) in which vaccine antigens are formulated. Particulate carriers like alum serve to promote the

uptake, processing and presentation of soluble antigens by macrophage. Alum, however, is not without side-effects and enhances humoral (antibody) immunity only.

An effective adjuvant potentiates both a humoral and cellular immune response in vaccinated animals. Further, an adjuvant must enhance a host's natural immune response and not aggravate the host system. A well-defined synthetic adjuvant free from extraneous matter which is stable and easy to manufacture would provide these qualities. Compounds that have been prepared and tested for adjuvanticity (Shimizu *et al.* 1985, Bulusu *et al.* 1992, Ikeda *et al.* 1993, Shimizu *et al.* 1994, Shimizu *et al.* 1995, Miyajima *et al.* 1996), however, often display toxic properties, are unstable and/or have unsubstantial immunostimulatory effects.

The discovery and development of effective adjuvants is essential for improving the efficacy and safety of existing vaccines. Adjuvants impart synthetic peptide and carbohydrate antigens with sufficient immunogenicity to insure the success of the synthetic vaccine approach. There remains a need for new compounds having potent immunomodulating effects.

Summary of the Invention

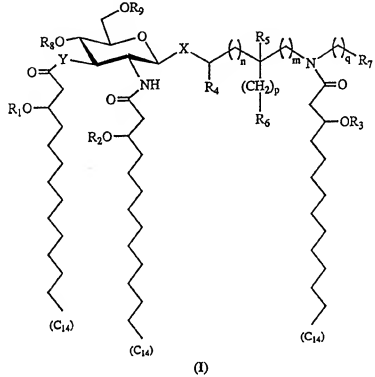
The compounds of the subject invention are aminoalkyl glucosamine phosphate compounds (AGPs) which are adjuvants and immunoeffectors. An aminoalkyl (aglycon) group is glycosidically linked to a 2-deoxy-2-amino-α-D-glucopyranose (glucosamine) to form the basic structure of the claimed molecules. The compounds are phosphorylated at the 4 or 6 carbon on the glucosamine ring. Further, the compounds possess three 3-alkanoyloxyalkanoyl residues.

The compounds of the subject invention are immunoeffector molecules augmenting antibody production in immunized animals, stimulating cytokine production and activating macrophage. In accordance with the subject invention, methods for using these compounds as adjuvants and immunoeffectors are disclosed.

Detailed Description of the Invention

The compounds of the subject invention are adjuvant and immunoeffector molecules which are aminoalkyl glucosamine phosphates (AGPs). The compounds

comprise a 2-deoxy-2-amino-α-D-glucopyranose (glucosamine) in glycosidic linkage with an aminoalkyl (aglycon) group. Compounds are phosphorylated at the 4 or 6 carbon on the glucosamine ring and have three alkanoyloxyalkanoyl residues. The compounds of the subject invention are described generally by Formula I,



(I)

wherein X represents an oxygen or sulfur atom, Y represents an oxygen atom or NH group, "n", "m", "p" and "q" are integers from 0 to 6, R_1, R_2, and R_3 represent normal fatty acyl residues having 7 to 16 carbon atoms, R_4 and R_5 are hydrogen or methyl, R_6 and R_7 are hydrogen, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl or carboxy and esters and amides thereof; R_8 and R_9 are phosphono or hydrogen. The configuration of the 3′ stereogenic centers to which the normal fatty acyl residues are attached is *R* or *S*, but preferably *R*. The stereochemistry of the carbon atoms to which R_4 or R_5 are attached can be *R* or *S*. All stereoisomers, both enantiomers and diastereomers, and mixtures thereof, are considered to fall within the scope of the subject invention.

The heteroatom X of the compounds of the subject invention can be oxygen or sulfur. In a preferred embodiment, X is oxygen. Although the stability of the molecules

could be effected by a substitution at X, the immunomodulating activity of molecules with these substitutions is not expected to change.

The number of carbon atoms between heteroatom X and the aglycon nitrogen atom is determined by variables "n" and "m". Variables "n" and "m" can be integers from 0 to 6. In a preferred embodiment, the total number of carbon atoms between heteroatom X and the aglycon nitrogen atom is from about 2 to about 6 and most preferably from about 2 to about 4.

The compounds of the subject invention are aminoalkyl glucosamine compounds which are phosphorylated. Compounds can be phosphorylated at position 4 or 6 (R_8 or R_9) on the glucosamine ring and are most effective if phosphorylated on at least one of these positions. In a preferred embodiment, R_8 is phosphono and R_9 is hydrogen.

The compounds of the subject invention are hexaacylated, that is they contain a total of six fatty acid residues. The aminoalkyl glucosamine moiety is acylated at the 2-amino and 3-hydroxyl groups of the glucosamine unit and at the amino group of the aglycon unit with 3-hydroxyalkanoyl residues. In Formula I, these three positions are acylated with 3-hydroxytetradecanoyl moieties. The 3-hydroxytetradecanoyl residues are, in turn, substituted with normal fatty acids (R_1-R_3), providing three 3-*n*-alkanoyloxytetradecanoyl residues or six fatty acid groups in total.

The chain length of normal fatty acids R_1-R_3 can be from about 7 to about 16 carbons. Preferably, R_1-R_3 are from about 9 to about 14 carbons. The chain lengths of these normal fatty acids can be the same or different. Although, only normal fatty acids are described, it is expected that unsaturated fatty acids (*i.e.* fatty acid moieties having double or triple bonds) substituted at R_1-R_3 on the compounds of the subject invention would produce biologically active molecules. Further, slight modifications in the chain length of the 3-hydroxyalkanoyl residues are not expected to dramatically effect biological activity.

The compounds of the subject invention are adjuvants and immunoeffectors which enhance the generation of antibody in immunized animals, stimulate the production of cytokines and stimulate a cell-mediated immune response including a cytotoxic T-lymphocyte response. In methods for effecting the immune response of an individual, the compounds of the subject invention can be formulated with a

pharmaceutically acceptable carrier for injection or ingestion. As used herein, "pharmaceutically acceptable carrier" means a medium which does not interfere with the immunomodulatory activity of the active ingredient and is not toxic to the patient to whom it is administered. Pharmaceutically acccptable carriers include oil-in-water or water-in-oil emulsions, aqueous compositions, liposomes, microbeads and microsomes.

Formulations of the compounds of the subject invention that can be administered parenterally, i.e. intraperitoneally, subcutaneously or intramuscularly include the following preferred carriers. Examples of preferred carriers for subcutaneous use include a phosphate buffered saline (PBS) solution and 0.01-0.1 % triethanolamine in USP Water for Injection. Suitable carriers for intramuscular injection include 10% USP ethanol, 40% propylene glycol and the balance an acceptable isotonic solution such as 5% dextrose. Examples of preferred carriers for intravenous use include 10% USP ethanol, 40% USP propylene glycol and the balance USP Water for Injection. Another acceptable carrier includes 10% USP ethanol and USP Water for Injection; yet another acceptable carrier is 0.01-0.1% triethanolamine in USP Water for Injection. Pharmaceutically acceptable parenteral solvents are such as to provide a solution or dispersion may be filtered through a 5 micron filter without removing the active ingredient.

Examples of carriers for administration via mucosal surfaces depend upon the particular route. When administered orally, pharmaceutical grades of mannitol, starch, lactose, magnesium stearate, sodium saccharide, cellulose, magnesium carbonate and the like, with mannitol being preferred. When administered intranasally, polyethylene glycol or glycols, sucrose, and/or methylcellulose, and preservatives such as benzalkonium chloride, EDTA, may be used, with polyethylene glycols being preferred, and when administered by inhalation, suitable carriers are polyethylene glycol or glycols, methylcellulose, dispensing agents, and preservatives, with polyethylene glycols being preferred.

The compounds of the subject invention are administered to an individual in "an effective amount" to effect or enhance the individual's immune response. As used herein, "an effective amount" is that amount which shows a response over and above the vehicle

or negative controls. The precise dosage of the compounds of the subject invention to be administered to a patient will depend upon the particular AGP used, the route of administration, the pharmaceutical composition, and the patient. For example, when administered subcutaneously to enhance an antibody response, the amount of AGP used is from 1 to about 250 micrograms, preferably from about 25 to about 50 micrograms based upon administration to a typical 70 kg adult patient.

In vaccine compositions, the AGPs of the subject invention are administered to a warm-blooded animal, including humans, with an antigen. The amount of antigen administered to elicit a desired response can be readily determined by one skilled in the art and will vary with the type of antigen administered, route of administration and immunization schedule. For example, 0.2 μg of tetanus toxoid administered with the claimed compounds subcutaneously to a mouse in two immunization 21 days apart elicited a humoral immune response to that antigen.

The compounds of the subject invention are synthesized by coupling an *N*-acyloxyacylated or *N*-protected aminoalkanol or aminoalkanethiol (aglycon unit) with a suitably protected and/or 3-*O*-acyloxyacylated glucosamine unit. In one preferred method for preparing the compounds of the subject invention (Scheme 1), an *N*-(2,2,2-trichloroethoxycarbonyl (Troc))-protected glycosyl halide **1** (Z = F, Cl, Br) is coupled with an *N*-[(*R*)-3-*n*-alkanoyloxytetradecanoyl]aminoalkanol or thiol **2** (possessing R_6 and R_7 in suitably protected form) via a Koenigs-Knorr type reaction in the presence of mercury or silver salts to give glycoside intermediate **3**. Preferably, the glucosamine unit **1** possesses an anomeric chloride atom (Z = Cl), and the coupling catalyst is silver trifluoromethanesulfonate. Intermediate **3** can also be prepared by coupling the aglycon unit **2** with an *N*-Troc-protected glycosyl acetate (Z = OAc) or related activated derivative in the presence of a Lewis acid such as boron trifluoride etherate. By "activated" is meant having an appropriate displaceable leaving group "Z" attached to the anomeric center of the glucosamine unit. Glucosamine unit **1** bears an (*R*)-3-*n*-alkanoyloxytetradecanoyl residue on the 3-position, and suitable protecting groups on the 6-hydroxyl and 4-phosphate moieties. Typical protecting groups for the phosphate group include, but are not limited to, phenyl, benzyl, and *o*-xylyl. The phosphate group is protected preferably with two phenyl groups. The 6-position can be temporarily

protected by blocking groups commonly used in sugar chemistry such as silyl, benzyl, or benzyloxymethyl ethers or, alternatively, an alkyl carbonate. The 6-hydroxyl group is protected preferably as a 1,1-dimethyl-2,2,2-trichloroethyl carbonate (TCBOC).

The trichloroethyl-based protecting group(s) in the Koenigs-Knorr coupled product **3** are removed with zinc and the glucosamine nitrogen is selectively acylated with a (*R*)-3-*n*-alkanoyloxytetradecanoic acid **4** in the presence of a suitable coupling reagent to give the hexaacylated derivative **5**. The remaining protecting groups in **5** are then cleaved by catalytic hydrogenation in the presence of a palladium or platinum catalyst or by other appropriate means to give compounds of Formula (I).

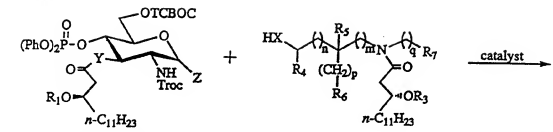
A suitable starting material for the synthesis of glycosyl donor **1** is 2-(trimethylsilyl)ethyl 2-amino-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside which can be prepared from commercially available D-glucosamine hydrochloride using published procedures. The conversion of the 2-(trimethylsilyl)ethyl glycoside starting material to glycosyl donor **1** can be achieved by methods known in the art or modifications thereof which are described herein. The aglycon unit **2** can be prepared by *N*-acyloxyacylation of commercially available starting materials with an appropriate (*R*)-3-*n*-alkanoyloxytetradecanoic acid **4**, or *N*-acyloxyacylation of starting materials that can be obtained by known methods in the chemical literature. Alternatively, the *N*-acyloxyacyl residue in **2** can be substituted with an appropriate amine protecting group which is removed subsequent to the coupling reaction such as is described in the second preferred embodiment below.

In a second preferred method for preparing the compounds of the subject invention (Scheme 2), introduction of the (*R*)-3-*n*-alkanoyloxytetradecanoyl and phosphate groups into the glucosamine and aglycon units is performed subsequent to the glycosylation (coupling) reaction using *N*- and *O*-protecting groups suitable for the chemical differentiation of the amino and hydroxyl groups present. Preferably, the *N*-Troc-protected glycosyl donor **6** is coupled with an *N*-allyloxycarbonyl (AOC)-protected aminoalkanol or thiol **7** in the presence of an appropriate catalyst to give the aminoalkyl β-glycoside **8**. Most preferably, the glycosyl donor **6** possesses an anomeric acetoxy group (Z = OAc), and the coupling catalyst is boron trifluoride etherate. Other *N*-protecting groups for the aglycon amino group include, but are not limited to,

commonly employed carbamates obvious to one skilled in the art such as *t*-butyl (*t*-BOC), benzyl (Cbz), 2,2,2-trichloroethyl (Troc), and 9-fluorenylmethyl(Fmoc).

Base-induced cleavage of the acetate groups in coupling product **8** and 4,6-acetonide formation under standard conditions known in the art gives intermediate **9**. 3-*O*-Acylation of **9** with (*R*)-3-*n*-alkanoyloxytetradecanoic acid **4**, followed by palladium(0)-mediated removal of the aglycon *N*-AOC group and *N*-acylation with (*R*)-3-*n*-alkanoyloxytetradecanoic acid **4** provides intermediate **10**. Acetonide hydrolysis and functionalization of the 4- and 6-positions as described herein for the preparation of glycosyl donor **1** gives intermediate **3** (Y=O) which is then processed as in Scheme 1 to afford compounds of general Formula (I).

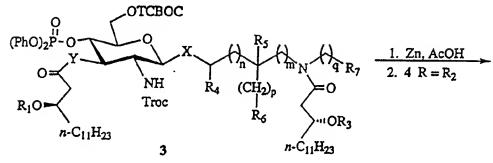
The present invention is further described by way of the following non-limiting Examples and Test Examples which are given for illustrative purposes only. It is important to note that the introduction of the (*R*)-3-*n*-alkanoyloxytetradecanoyl groups and the phosphate group(s) into the glucosamine and aglycon units do not necessarily have to be performed in the order shown in Schemes 1 and 2 or described in the Examples shown below.



1 Z = halide, OAc, etc, Y = O, NH

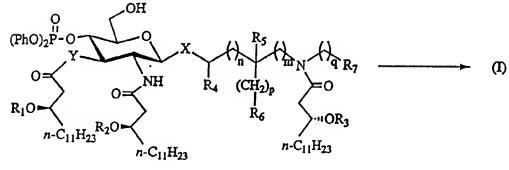
2

catalyst



3

1. Zn, AcOH
2. 4 R = R_2



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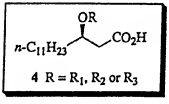
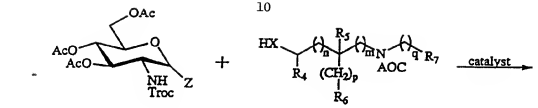
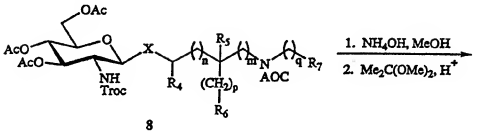


4 R = R_1, R_2 or R_3

Scheme 1



6 Z = halide, OAc, etc. 7



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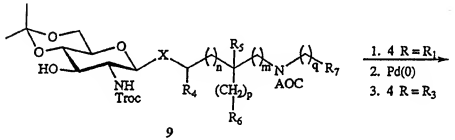

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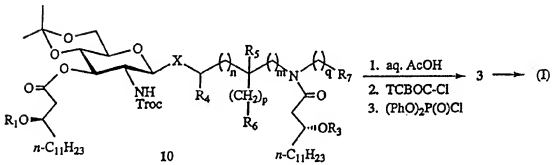

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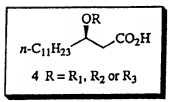

4 R = R_1, R_2 or R_3

Scheme 2

Examples 1-29 describe methods of making the AGP compounds of the subject invention. Test Examples 1-7 describe assays conducted to the determine the immunogenicity of these compounds. Table 1 lists the chemical composition and experimental reference numbers for each compound in these examples.

5

Table 1.

Example	Ref. No.	R_1-R_3	n	p	R_6	q	R_7
1	-	-	-	-	-	-	-
2	B1*	*n*-$C_{13}H_{27}CO$	0	1	OH	0	H
3	B2**	*n*-$C_{13}H_{27}CO$	0	1	OH	0	H
4	B3	*n*-$C_{11}H_{23}CO$	0	1	OH	0	H
5	B4	*n*-$C_{10}H_{21}CO$	0	1	OH	0	H
6	B5	*n*-$C_9H_{19}CO$	0	1	OH	0	H
7	B6***	*n*-$C_9H_{19}CO$	0	1	OH	0	H
8	B7	*n*-$C_8H_{17}CO$	0	1	OH	0	H
9	B8	*n*-$C_6H_{13}CO$	0	1	OH	0	H
10	B9	*n*-$C_9H_{19}CO$	1	1	OH	0	H
11	B10	*n*-$C_9H_{19}CO$	0	2	OH	0	H
12	B11	*n*-$C_{13}H_{27}CO$	0	0	CO_2H	0	H
13	B12	*n*-$C_{11}H_{23}CO$	0	0	CO_2H	0	H
14	B13	*n*-$C_{10}H_{21}CO$	0	0	CO_2H	0	H
15	B14**	*n*-$C_9H_{19}CO$	0	0	CO_2H	0	H
16	B15*	*n*-$C_9H_{19}CO$	0	0	CO_2H	0	H

Table 1 continued.

Example	Ref. No.	R_1-R_3	n	p	R_6	q	R_7
17	B16	n-$C_8H_{17}CO$	0	0	CO_2H	0	H
18	B17	n-$C_7H_{15}CO$	0	0	CO_2H	0	H
19	B18	n-$C_6H_{13}CO$	0	0	CO_2H	0	H
20	B19	n-$C_{13}H_{27}CO$	0	0	H	0	H
21	B20	n-$C_9H_{19}CO$	0	0	H	0	H
22	B21	n-$C_{13}H_{27}CO$	1	0	H	0	H
23	B22	n-$C_{13}H_{27}CO$	2	0	H	0	H
24	B23	n-$C_{13}H_{27}CO$	4	0	H	0	H
25	B24	n-$C_{13}H_{27}CO$	0	0	$CONH_2$	0	H
26	B25	n-$C_9H_{19}CO$	0	0	$CONH_2$	0	H
27	B26	n-$C_{13}H_{27}CO$	0	0	CO_2Me	0	H
28	B27	n-$C_{13}H_{27}CO$	0	0	H	1	CO_2H
29	B28	n-$C_9H_{19}CO$	1	0	H	1	CO_2H

For all Examples shown: X=Y=O; R_4=R_5=H; m=0; R_8=phosphono; R_9=H.
*the stereochemistry of the carbon atom to which R_5 is attached is S.
**the stereochemistry of the carbon atom to which R_5 is attached is R.
***R_8 is H and R_9 is phosphono.

EXAMPLE 1

Preparation of (*R*)-3-*n*-alkanoyloxytetradecanoic acids (4).

(1) A solution of methyl 3-oxotetradecanoate (19 g, 0.074 mol) in MeOH (100 mL) was degassed by sparging with argon (15 min). [(*R*)-Ru(Binap)Cl]$_2$·NEt$_3$ catalyst (0.187 g, 0.111 mmol) and 2 N aqueous HCl (0.5 mL) were added and the resulting mixture was hydrogenated at 60 psig and 40-50°C for 18 h. The reaction was diluted with hexanes (250 mL), filtered through a short column of silica gel, and concentrated. The crude product was dissolved in tetrahydrofuran (THF; 200 mL), treated 2.4 N aqueous LiOH (83 mL, 0.2 mol) and stirred vigorously at room temperature for 4 h. The resulting slurry was partitioned between ether (200 mL) and 1 N aqueous HCl (200 mL) and the layers separated. The aqueous layer was extracted with ether (100 mL) and the combined ethereal extracts were dried (Na_2SO_4) and concentrated. The crude hydroxy acid was dissolved in hot acetonitrile (250 mL), treated with dicyclohexylamine (DCHA; 17 mL, 0.085 mol) and stirred at 60°C for 1 h. The product that crystallized upon cooling was collected and recrystallized from acetonitrile (650 mL) to yield 28.6 g (91%) of dicyclohexylammonium (*R*)-3-hydroxytetradecanoate as a colorless solid: mp 94-95°C; ^{1}H NMR ($CDCl_3$) δ 0.88 (~t, 3 H, *J* ~ 6.5 Hz), 1.05-1.58 (m, 24 H), 1.65 (m, 2 H), 1.80 (m, 4 H), 2.01 (br d, 4 H) 2.18 (dd, 1 H, *J* = 15.7, 9.4 Hz), 2.36 (dd, 1 H, *J* = 15.7, 2.6 Hz), 2.94 (m, 2 H), 3.84 (m, 1 H)

(2) To a mixture of the compound prepared in (1) above (50 g, 0.117 mol) and 2,4′-dibromoacetophenone (39 g, 0.14 mol) in EtOAc (2.3 L) was added triethylamine (19.6 mL, 0.14 mol) and the resulting solution was stirred for 18 h at room temperature. The voluminous precipitate that formed was collected and triturated with warm EtOAc (3 x 400 mL). The combined triturates and filtrate were washed with 1 M aq. HCl, saturated aq. NaCl and dried (Na_2SO_4). Volatiles were removed under reduced pressure and the crude product obtained was crystallized from EtOAc-hexanes to give 47.2 g (91%) of (*R*)-3-hydroxytetradecanoic acid *p*-bromophenacyl ester as a colorless solid: mp 109-109.5°C; ^{1}H NMR ($CDCl_3$) δ 0.88 (~t, 3 H, *J* ~ 6.5 Hz) 1.15-1.70 (m, 20 H), 2.56 (dd, 1 H, *J* = 15.1, 9.1 Hz), 2.69 (dd, 1 H, *J* = 15.1, 2.9 Hz), 3.27 (br s, 1 H), 4.12 (m, 1 H), 5.31 (d, 1 H, *J* = 16.5 Hz), 5.42 (d, 1 H, *J* = 16.5 Hz), 7.65 (d, 2 H, *J* = 8.5 Hz), 7.78 (d, 2 H, *J* = 8.5 Hz).

(3) A solution of the compound prepared in (2) above (4.6 g, 10.4 mmol) in CH_2Cl_2 (50 mL) containing 4-dimethylaminopyridine (0.12 g, 1.0 mmol) and pyridine (5 mL, 62 mmol) was treated at room temperature with myristoyl chloride (3.1 mL, 11.4 mmol). After stirring for 5 h at room temperature MeOH (0.5 mL) was added, and the reaction mixture was concentrated. The residue was partitioned between Et_2O (150 mL) and cold 10% aqueous HCl (50 mL) and the layers separated. The ethereal layer was dried (Na_2SO_4) and concentrated and the residue obtained was purified on a short pad of silica gel with 5% EtOAc-hexanes. The diester was dissolved in AcOH (42 mL) and treated with three equal portions of zinc dust (~6 g, 90 mmol) at 60°C over a 1 h period. After an additional hour at 60°C, the cooled reaction mixture was sonicated (5 min), filtered through Celite® and concentrated. The residue was purified by flash chromatography on silica gel with 10% EtOAc-hexanes to give 4.17 g (82%) of (*R*)-3-tetradecanoyloxytetradecanoic acid as a colorless solid: mp 28-29°C; ^1H NMR ($CDCl_3$) δ 0.88 (~t, 6 H), 1.15-1.40 (m, 38 H), 1.50-1.70 (m, 4 H), 2.28 (t, 2 H, *J* = 7.4 Hz), 2.56 (dd, 1 H, *J* = 15.9, 5.8 Hz), 2.63 (dd, 1 H, *J* = 15.9, 7.1 Hz), 5.21 (m, 1 H).

(4) In the same manner as described in Example 1-(3), the compound prepared in Example 1-(2) (2.5 g, 5.68 mmol) was acylated with lauroyl chloride (1.45 mL, 6.25 mmol) in the presence of pyridine (0.57 mL, 7.0 mmol) in CH_2Cl_2 (60 mL) and then deprotected with zinc (9.3 g, 142 mmol) in AcOH (40 mL) to afford (*R*)-3-dodecanoyloxytetradecanoic acid as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.90 (t, 6 H, *J* = 6.5 Hz), 1.0 - 1.75 (m, 46 H), 2.30 (m, 2 H), 2.62 (m, 2 H), 5.22 (m, 1 H).

(5) A solution of the compound prepared in Example 1-(2) (2.5 g, 5.68 mmol) was treated with undecanoic acid (1.16 g, 6.25 mmol) and EDC·MeI (2.08 g, 7.0 mmol) in CH_2Cl_2 (60 mL) and then deprotected as described in Example 1-(3) with zinc (9.3 g, 142 mmol) in AcOH (40 mL) to afford (*R*)-3-undecanoyloxytetradecanoic acid as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.89 (t, 6 H, *J* = 6.7 Hz), 1.0 - 1.75 (m, 44 H), 2.29 (m, 2 H), 2.61 (m, 2 H), 5.22 (m, 1 H).

(6) In the same manner as described in Example 1-(3), the compound prepared in Example 1-(2) (4.4 g, 10 mmol) was acylated with decanoyl chloride (2.3 mL, 11 mmol) in the presence of pyridine (1.2 mL, 15.0 mmol) in CH_2Cl_2 (100 mL) and then deprotected with zinc (16.4 g, 250 mmol) in AcOH (60 mL) to afford (*R*)-3-

decanoyloxytetradecanoic acid as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 6 H, J = 6.8 Hz), 1.0 - 1.75 (m, 34 H), 2.29 (t, 2 H, J = 7.4 Hz), 2.61 (t, 2 H, J = 4.2 Hz), 5.22 (m, 1 H).

(7) In the same manner as described in Example 1-(3), the compound prepared in Example 1-(2) (2.5 g, 5.68 mmol) was acylated with nonanoyl chloride (1.13 mL, 6.25 mmol) in the presence of pyridine (0.57 mL, 7.0 mmol) in CH_2Cl_2 (60 mL) and then deprotected with zinc (9.3 g, 142 mmol) in AcOH (40 mL) to afford (*R*)-3-nonanoyloxytetradecanoic acid as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 6 H, J = 6.9 Hz), 1.0 - 1.75 (m, 32 H), 2.29 (t, 2 H, J = 7.5 Hz), 2.61 (m, 2 H), 5.22 (m, 1 H).

(8) In the same manner as described in Example 1-(3), the compound prepared in Example 1-(2) (2.5 g, 5.68 mmol) was acylated with octanoyl chloride (1.07 mL, 6.25 mmol) in the presence of pyridine (0.57 mL, 7.0 mmol) in CH_2Cl_2 (60 mL) and then deprotected with zinc (9.3 g, 142 mmol) in AcOH (40 mL) to afford (*R*)-3-octanoyloxytetradecanoic acid as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 6 H, J = 6.9 Hz), 1.0 - 1.75 (m, 30 H), 2.32 (t, 2 H, J = 7.4 Hz), 2.63 (t, 2 H, J = 4.4 Hz), 5.23 (m, 1 H).

(9) In the same manner as described in Example 1-(3), the compound prepared in Example 1-(2) (2.5 g, 5.68 mmol) was acylated with heptanoyl chloride (0.97 mL, 6.25 mmol) in the presence of pyridine (0.57 mL, 7.0 mmol) in CH_2Cl_2 (60 mL) and then deprotected with zinc (9.3 g, 142 mmol) in AcOH (40 mL) to afford (*R*)-3-heptanoyloxytetradecanoic acid as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 6 H, J = 6.8 Hz), 1.0 - 1.75 (m, 28 H), 2.29 (t, 2 H, J = 7.4 Hz), 2.61 (d, 2 H, J = 5.8 Hz), 5.22 (m, 1 H).

EXAMPLE 2 (B1)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) To a solution of 2-(trimethylsilyl)ethyl 2-amino-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (6.46 g, 20.2 mmol) in $CHCl_3$ (300 mL) was added

1 N aqueous $NaHCO_3$ (300 mL) and 2,2,2-trichloroethyl chloroformate (8.5 g, 40 mmol). The resulting mixture was stirred vigorously for 3 h at room temperature. The organic layer was separated, dried (Na_2SO_4) and concentrated to give a colorless syrup. Flash chromatography on silica gel (gradient elution, 30→40% EtOAc-hexanes) afforded 9.6 g (96%) of 2-(trimethylsilyl)ethyl 2-deoxy-4,6-*O*-isopropylidine-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless solid: mp 69-70°C; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.94 (m, 2 H), 1.44 and 1.52 (2s, 6 H), 2.94 (br s, 1 H), 3.23-3.37 (m, 2 H), 3.48-3.62 (m, 2 H), 3.79 (t, 1 H, J = ~10.5 Hz), 3.88-4.08 (m, 3 H), 4.65 (d, 1 H, J=8.3 Hz), 4.74 (m, 2 H), 5.39 (d, 1 H, J=7.4 Hz).

(2) A solution of the compound prepared in (1) above (7.5 g, 15.2 mmol), (*R*)-3-tetradecanoyloxytetradccanoic acid (7.58 g, 16.7 mmol) and 4-pyrrolidinopyridine (0.25 g, 1.7 mmol) in CH_2Cl_2 (95 mL) was treated with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide methiodide (EDC·MeI; 4.94 g, 16.7 mmol) and stirred for 16 h at room temperature. The reaction mixture was filtered through a short pad of Celite®, concentrated, and the resulting residue was heated at 60°C in 90% aqueous AcOH (100 mL) for 1 h. The mixture was concentrated and residual AcOH and water were removed by azeotroping with toluene (2 x 150 mL). The crude diol was purified by flash chromatography on silica gel (gradient elution, 30→40% EtOAc-hexanes) to give 11.8 g (83%) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.9 (m, 8 H), 1.1-1.7 (m, 42 H), 2.30 (t, 2 H, J=7.4 Hz), 2.52 (m, 2 H), 3.36-3.72 (m, 4 H), 3.78-4.03 (m, 3 H), 4.57 (d, 1 H, J=8.3 Hz), 4.65 (d, 1 H, J=11 Hz), 4.77 (d, 1 H, J=11 Hz), 5.0-5.15 (m, 2 H), 5.20 (d, 1 H, J=7.4 Hz).

(3) A solution of the compound prepared in (2) above (10.9 g, 12 mmol) and pyridine (2 mL, 25 mmol) in CH_2Cl_2 (125 mL) at 0°C was treated dropwise over 15 min with a solution of 2,2,2-trichloro-1,1-dimethylethyl chloroformate (3.17 g, 13.2 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was allowed to warm slowly to ambient temperature over 3.5 h. 4-Pyrrolidinopyridine (0.89 g, 6.0 mmol), *N,N*-diisopropylethylamine (10.5 mL, 60 mmol) and diphenyl chlorophosphate (3.7 mL, 18 mmol) were added sequentially and the resulting mixture was stirred for 5 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (500 mL), washed with cold

7.5% aqueous HCl (2 x 250 mL), water (250 mL), saturated aqueous $NaHCO_3$ (250 mL), dried (Na_2SO_4), and then concentrated. The residue obtained was purified by flash chromatography on silica gel eluting with 12.5% EtOAc-hexanes to give 15.1 g (95%) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichlorethoxycarbonylamino)-β-D-glucopyranoside as a viscous oil: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.8-1.0 (m, 8 H), 1.1-1.65 (m, 42 H), 1.83 and 1.90 (2s, 6 H), 2.15-2.45 (m, 4 H), 3.34 (q, 1 H, *J* = ~8 Hz), 3.37 (m, 1 H), 3.81 (m, 1 H), 3.95 (m, 1 H), 4.27 (dd, 1 H, *J*=12, 5 Hz), 4.34 (d, 1 H, *J*=12 Hz), 4.58 (d, 1 H, *J*=12 Hz), 4.66 (q, 1 H, *J*= ~9 Hz), 4.86 (d, 1 H, *J*=12 Hz), 5.03 (d, 1 H, *J*=7.9 Hz), 5.21 (m, 1 H), 5.54-5.70 (m, 2 H), 7.2-7.8 (m, 10 H).

(4) A solution of the compound prepared in (3) above (1.87 g, 1.41 mmol) in CH_2Cl_2 (3 mL) at 0°C was treated dropwise over 10 min with trifluoroacetic acid (TFA; 6 mL) and then stirred for 4 h at 0°C. The reaction mixture was concentrated and residual TFA was removed by azeotroping with toluene (2 x 5 mL). A solution of the lactol and dimethylformamide (2.2 mL, 28.2 mmol) in CH_2Cl_2 (14 mL) at 0°C was treated with oxalyl bromide (2.0 M in CH_2Cl_2; 2.1 mL, 4.2 mmol) dropwise over 15 min and the resulting suspension was stirred at 0°C for 24 h. The reaction mixture was partitioned between cold saturated aqueous $NaHCO_3$ (25 mL) and ether (50 mL) and the layers were separated. The ethereal layer was washed with saturated aqueous NaCl, dried (Na_2SO_4) and concentrated to give 1.85 g (~100%) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl bromide as a colorless glass.

(5) A solution of (*R*)-2-amino-3-benzyloxy-1-propanol (0.46 g, 2.33 mmol) and (*R*)-3-tetradecanoyloxytetradecanoic acid (1.29 g, 2.83 mmol) in CH_2Cl_2 (20 mL) was treated with EDC·MeI (0.78 g, 2.79 mmol) and stirred for 16 h at room temperature. The reaction mixture was filtered through a short pad of Celite® and concentrated. Flash chromatography on silica gel with 45% EtOAc-hexanes afforded 1.1 g (69%) of 3-benzyloxy-(*R*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propanol as a colorless solid: mp 42-44.5°C; ^{1}H NMR δ 0.88 (t, 6 H, *J* = ~6.5 Hz), 1.0-1.7 (m, 42 H), 2.50 (t, 2

H, *J*=7.5 Hz), 2.46 (m, 2 H), 3.56 (br s, 1 H), 3.5-3.75 (m, 3 H), 3.78 (dd, 1 H, *J*=11, 4 Hz), 4.08 (m, 1 H), 4.51 (s, 2 H), 5.17 (m, 1 H), 6.36 (d, 1 H, *J*=7.8 Hz), 7.2-7.4 (m, 5 H).

(6) To a solution of the compound prepared in (4) above (1.00 g, 0.776 mmol) and the compound prepared in (5) above (0.35 g, 0.57 mmol) in dichloroethane (4.5 mL) was added powdered 4 Å molecular sieves (1.25 g) and calcium sulfate (2.7 g, 20 mmol). After stirring for 10 min at room temperature, the mixture was treated with mercury cyanide (1.0 g, 4.0 mmol) and then heated to reflux for 12 h shielded from light. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and filtered through a pad of Celite®. The filtrate was washed with 1 N aqueous KI (25 mL), dried (Na_2SO_4) and concentrated. The residue was chromatographed on silica gel with EtOAc-hexanes-MeOH (80:20:0→70:30:1, gradient elution) to give 0.66 g (63%) of 3-benzyloxy-(*S*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR δ 0.88 (t, 12 H, *J*= ~6.5 Hz), 1.0-1.65 (m, 84 H), 1.79 and 1.86 (2s, 6 H), 2.1-2.5 (m, 8 H), 3.35-3.55 (m, 3 H), 3.65-3.8 (m, 3 H), 4.1-4.75 (m, 9 H), 5.05-5.3 (m, 2 H), 5.3-5.5 (m, 2 H), 6.04 (d, 1 H, *J*=8.4 Hz), 7.05-7.45 (m, 15 H).

(7) A stirred solution of the compound prepared in (6) above (0.60 g, 0.328 mmol) in AcOH (9 mL) at 55°C was treated with zinc dust (1.1 g, 16 mmol) in three equal portions over 1 h. The cooled reaction mixture was sonicated, filtered through a bed of Celite® and concentrated. The resulting residue was partitioned between CH_2Cl_2 (60 mL) and cold 1 N aqueous HCl (35 mL) and the layers separated. The organic layer was washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4) and concentrated. A mixture of the residue obtained and (*R*)-3-tetradecanoyloxytetradecanoic acid (0.18 g, 0.39 mmol) in CH_2Cl_2 (3.5 mL) was stirred with powdered 4Å molecular sieves (0.1 g) for 30 min at room temperature and then treated with 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ; 0.12 g, 0.49 mmol). The resulting mixture was stirred for 6 h at room temperature, filtered through Celite® and then concentrated. Chromatography on silica gel (gradient elution, 0.5→1% MeOH-$CHCl_3$) afforded 0.31 g (50%) of 3-benzyloxy-(*S*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-

tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 18 H, *J*= ~6.5 Hz), 1.0-1.8 (m, 126 H), 2.1-2.5 (m, 12 H), 3.35-3.75 (m, 6 H), 3.80 (m, 2 H), 4.23 (m, 1 H), 4.46 (d, 1 H, *J*=12 Hz), 4.51 (d, 1 H, *J*=12 Hz), 4.65 (q, 1 H, *J*= ~9.5 Hz), 4.82 (d, 1 H, *J*=8.1 Hz), 5.05-5.25 (m, 3 H), 5.47 (t, 1 H, *J*= ~9.5 Hz), 6.16 (d, 1 H, *J*=8.1 Hz), 6.31 (d, 1 H, *J*=8.4 Hz), 7.1-7.4 (m, 15 H).

(8) A solution of the compound prepared in (7) above (0.26 g, 0.138 mmol) in THF (25 mL) was hydrogenated in the presence of 5% palladium on carbon (50 mg) at room temperature and atmospheric pressure for 16 h. After removal of the catalyst by filtration, AcOH (3 mL) and platinum oxide (0.14 g) were added and the hydrogenation was continued at room temperature and 75 psig for 24 h. The resulting opalescent reaction mixture was diluted with 2:1 $CHCl_3$-MeOH (20 mL) and sonicated briefly to give a clear solution. The catalyst was collected, washed with 2:1 $CHCl_3$-MeOH (2 x 5 mL) and the combined filtrate and washings were concentrated. The residue was dissolved in 1% aqueous triethylamine (10 mL) by sonicating for 5 min at 35°C and the resulting solution was lyophilized. Flash chromatography on silica gel with chloroform-methanol-water-triethylamine (94:6:0.5:0.5→88:12:1.0:1.0, gradient elution) afforded 0.20 g (84%) of product as a colorless powder. A portion of the chromatography product (0.166 g) was dissolved in cold 2:1 $CHCl_3$-MeOH (33 mL) and washed with cold 0.1 N aqueous HCl (14 mL). The lower organic layer was filtered and concentrated and the free acid obtained was lyophilized from 1% aqueous triethylamine (pyrogen free, 15 mL) to give 0.160 g of 3-hydroxy-(*S*)-2-[(*R*)-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a colorless solid: mp 178-180°C (dec); IR (film) 3293, 3103, 2959, 2924, 2855, 1732, 1654, 1640, 1553, 1467, 1377, 1259, 1175, 1106, 1086, 1050, 803, 720 cm^{-1}; HMR ($CDCl_3$—CD_3OD) δ 0.88 (t, 18 H, *J*= ~7 Hz), 1.0-1.7 (m, 135 H), 2.15-2.75 (m, 12 H), 3.02 (q, 6 H, *J*=7 Hz), 3.35-4.1 (m, 7 H), 4.22 (q, 1 H, *J* =~ 9.5 Hz), 4.77 (d, 1 H, *J*=8 Hz), 5.05-5.35 (m, 4 H), 6.58 (d, 1 H, *J*= 6 Hz), 6.73 (d, 1 H, *J*= 7.5 Hz, NH); ^{13}C NMR ($CDCl_3$) δ 173.5, 173.2, 170.7, 170.5, 170.0, 100.7, 75.9, 72.7, 71.2, 71.0, 70.8, 70.6, 67.9, 61.7, 60.5, 55.0, 50.4, 45.6, 41.4, 39.5, 34.5, 34.4, 32.0, 31.8, 30.3, 29.8, 29.4, 29.3, 25.3, 25.1, 22.7, 14.2, 8.6.

Anal. Calcd for $C_{19}H_{192}N_3O_{18}P \cdot 5\ H_2O$: C, 64.84; H, 11.10; N, 2.29; P, 1.69. Found: C, 64.69; H, 11.24; N, 1.93; P, 1.44.

EXAMPLE 3 (B2)

Preparation of 3-Hydroxy-(*R*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) A solution of the compound prepared in Example 2-(5) (0.63 g, 1.02 mmol) in CH_2Cl_2 (7 mL) was treated sequentially with pyridine (0.4 mL, 5 mmol), 4-dimethylaminopyridine (cat.) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (0.307 g, 1.23 mmol) and stirred for 16 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (25 mL), washed with saturated aqueous $NaHCO_3$ (25 mL) and dried (Na_2SO_4). Removal of volatiles in vacuo gave a residuc which was dissolved in THF-AcOH (10 mL, 9:1) and hydrogenated in the presence of 5% palladium on carbon (150 mg) at room temperature and atmospheric pressure for 24 h. After removal of the catalyst by filtration and concentration of the filtrate, the residue was purified by flash chromatography on silica gel with 35% EtOAc-hexanes to give 0.536 g (72%) of 3-(2,2,2-trichloro-1,1-dimethylethoxycarbonyloxy)-(*S*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propanol as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J*= ~6.5 Hz), 1.1-1.7 (m, 42 H), 1.94 (s, 6 H), 2.30 (t, 2 H, *J*=7.5 Hz), 2.47 (d, 2 H, *J*=6 Hz), 3.50 (br s, 1 H), 3.72 (m, 2 H), 4.15-4.35 (m, 3 H), 5.15 (m, 1 H), 6.18 (d, 1 H, *J*=7.2 Hz).

(2) In the same manner as described in Example 2-(6), the compound prepared in (1) above (0.310 g, 0.426 mmol) and thc compound prepared in Example 2-(4) (0.961 g, 0.745 mmol) were coupled in the presence of mercury cyanide (0.43 g, 1.7 mmol) to give 0.644 g (78%) of 3-(2,2,2-trichloro-1,1-dimethylethyloxycarbonyloxy)-(*S*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J*= ~6.5 Hz), 1.0-1.7 (m, 84 H), 1.81 and 1.89 (2s, 6 H),

1.93 (s, 6 H), 2.15-2.55 (m, 8 H), 3.45-3.7 (m, 2 H), 3.80 (br d, 1 H, *J*=9 Hz), 3.9-4.45 (m_r 6 H), 4.6-4.8 (m, 3 H), 4.87 (d, 1 H, *J*=8.1 Hz), 5.0-5.25 (m, 2 H), 5.48 (t, 1 H, *J*= ~9.5 Hz), 6.1-6.3 (m, 2 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (0.602 g, 0.310 mmol) was deprotected with zinc (1.5 g, 23 mmol) and acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid, (0.17 g, 0.37 mmol) in the presence of EEDQ (0.115 g, 0.467 mmol) to give 0.365 g (66%) of 3-hydroxy-(*R*)-2-[(*R*)-3-tctradccanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 18 H, *J*= ~6.5 Hz), 1.0-1.7 (m, 126 H), 2.15-2.55 (m, 12 H), 3.18 (br s, 1 H), 3.45-3.8 (m, 8 H), 3.85-4.05 (m, 2 H), 4.69 (q, 1 H, *J*= ~9.5 Hz), 5.05-5.25 (m, 3 H), 5.42 (t, 1 H, *J*=~9.5 Hz), 6.42 (d, 1 H, *J*=7.8 Hz), 6.59 (d, 1 H, *J*=7.2 Hz), 7.1-7.4 (m, 10 H).

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (0.355 g, 0.196 mmol) was hydrogenated in the presence of platinum oxide (175 mg) to give 0.265 g (77%) of 3-hydroxy-(*R*)-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a colorless solid: mp 159-160°C; IR (film) 3291, 2956, 2922, 2853, 1738, 1732, 1716, 1650, 1643, 1556, 1468, 1171, 1109, 1083, 1051 cm^{-1}; ^{1}H NMR ($CDCl_3$-CD_3OD) δ 0.88 (t, 18 H, *J*= ~6.5 Hz), 1.0-1.7 (m, 135 H), 2.15-2.75 (m, 12 H), 3.06 (q, 6 H, *J*=7 Hz), 3.25-3.45 (m, 2 H), 3.5-4.05 (m, 12 H), 4.19 (q, 1 H, *J*= ~ 9.5 Hz), 4.48 (d, 1 H, *J*=8.4 Hz), 5.04-5.26 (m, 4 H), 7.18 (d, 1 H, *J*=7.8 Hz), 7.27 (d, 1 H, *J*=8.7 Hz); ^{13}C NMR ($CDCl_3$) δ 173.5, 173.4, 170.7, 170.6, 170.1, 101.0, 76.0, 72.6, 71.4, 71.0, 70.8, 70.6, 68.7, 61.8, 60.5, 55.3, 50.5, 45.6, 41.5, 41.4, 39.5, 34.6, 34.4, 34.3, 32.0, 29.8, 29.4, 25.4, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd for $C_{99}H_{192}N_3O_{18}P \cdot H_2O$: C, 67.50; H, 11.10; N, 2.39; P, 1.76. Found: C, 67.40; H, 11.22; N, 2.34; P, 2.11.

EXAMPLE 4 (B3)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_{11}H_{23}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) A solution of D-glucosamine hydrochloride (20 g, 92.8 mmol) in H_2O (250 mL) was treated with a saturated aqueous $NaHCO_3$ (250 mL) and 2,2,2-trichloroethyl chloroformate (14.05 mL, 102 mmol) and stirred vigorously for 18 h. The white solid that formed was collected on a fritted funnel and dried under vacuum for 24 h. A solution of the solid in pyridine (100 mL) was cooled to 0 °C and treated with acetic anhydride (100 mL) via addition funnel. The solution was stirred for 18 h at room temperature, poured into 1 L of H_2O and extracted with $CHCl_3$ (3 x 500 mL). The solvent was removed *in vacuo* to afford 45 g (quant.) of *N*-(2,2,2-trichloroethoxycarbonylamino)-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranoside which was used without furthur purification: ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 6 H), 2.12 (s, 3 H), 2.22 (s, 3 H), 4.03 (m, 1 H), 4.07 (d, 1 H, *J* = 12.4 Hz), 4.22 (dt, 1 H, *J* = 9.9, 3.6 Hz), 4.30 (dd, 1 H, *J* = 12.4, 4.0 Hz), 4.64 (d, 1 H, *J* = 9.6 Hz), 5.28 (dt, 1 H, *J* = 10.2, 9.9 Hz), 6.25 (d, 1 H, *J* = 3.6 Hz).

(2) A solution of (*R*)-2-amino-3-benzyloxy-1-propanol (5 g, 27.6 mmol) in CH_2Cl_2 (250 mL) was treated with allyl chloroformate (3.2 mL, 30 mmol) and saturated aqueous $NaHCO_3$ (250 mL) for 18 h. The organic layer was separated and concentrated *in vacuo*. Purification by chromatography eluting with 30 % EtOAc / hexanes afforded 6.9 g (94 %) of (*R*)-2-(allyloxycarbonylamino)-3-benzyloxy-1-propanol as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.56 (br s, 1 H), 3.69 (m, 3 H), 3 88 (m, 2 H), 4.54 (s, 2 H), 4.58 (d, 2 H, *J* = 5.6 Hz), 5.23 (dd, 1 H, *J* = 10.4, 1.1 Hz), 5.33 (dd, 1 H, *J* = 17.1, 1.1 Hz), 5.42 (m, 1 H), 5.93 (m, 1 H), 7.35 (m, 5 H).

(3) A solution of the compounds prepared in (1) and (2) above (8.9 g, 17 mmol and 3.6 g, 10 mmol, respectively) in CH_2Cl_2 was treated with boron trifluoride etherate (4.3 mL, 34 mmol) at room temperature for 16 h. The reaction mixture was quenched with saturated aq. $NaHCO_3$ (100 mL) and extracted with EtOAc (3 x 100 mL). The combined EtOAc extracts were dreid (Na_2SO_4) and concentrated. The residue

obtained was chromatographed with 20 % EtOAc / hexanes to afford 6.03 g (83 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-3,4,6-tri-*O*-acetyl-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.02 (s, 3 H), 2.03 (s, 3 H), 2.08 (s, 3 H), 3.45 (m, 1 H), 3.54 (m, 1 H), 3.64 (m, 1 H), 3.76 (d, 1 H, *J* = 7.2 Hz), 3.91 (m, 2 H), 4.12 (d, 1 H, *J* = 12.2 Hz), 4.26 (dd, 1 H, *J* = 12.4, 4.7 Hz), 4.37 (d, 1 H, *J* = 8.2 Hz), 4.43 (d, 1 H, *J* = 12.1 Hz), 4.55 (m, 2 H), 4.68 (m, 2 H), 4.87 (d, 1 H, *J* = 8.0 Hz), 5.07 (m, 2 H), 5.21 (d, 1 H, *J* = 9.7 Hz), 5.29 (d, 1 H, *J* = 17.3 Hz), 5.91 (m, 1 H), 7.36 (m, 5 H).

(4) A solution of the compound prepared in (3) above (6.0 g, 8.3 mmol) in methanol (83 mL) was treated with ammonium hydroxide (8.3 mL) at room temperature for 2 h. The solvent was removed *in vacuo* and replaced with 2,2-dimethoxypropane (50 mL) and camphorsulfonic acid (100 mg) was added. The reaction was stirred for 18 h, neutralized with solid $NaHCO_3$ (1 g), filtered and concentrated *in vacuo*. Purification by chromatography with 50 % EtOAc / hexanes afforded 4.58 g (86 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-isopropylidine-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside: ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 3 H), 1.53 (s, 3 H), 2.94 (m, 1 H), 3.25 (m, 1 H), 3.55 (m, 4 H), 3.83 (m, 3 H), 3.93 (m, 3 H), 4.52 (m, 5 H), 4.68 (d, 1 H, *J* = 12.1 Hz), 4.77 (d, 1 H, *J* = 12.1 Hz), 5.07 (m, 1 H), 5.26 (m, 2 H), 5.92 (m, 1 H), 7.37 (m, 5 H).

(5) A solution of the compound prepared in (4) above (1.0 g, 1.56 mmol) in CH_2Cl_2 (20 mL) was treated with (*R*)-3-dodecanoyloxytetradecanoic acid (730 mg, 1.71 mmol) in the presence of EDC·MeI (560 mg, 1.87 mmol) and 4-pyrrolidinopyridine (50 mg). The reaction was stirred at room temperature for 18 h and filtered through a 6 x 8 cm plug of silica gel using 20 % EtOAc / hexanes as eluent to afford 1.33 g (82 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.8 Hz), 1.1 - 1.6 (m, 38 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.28 (t, 2 H, *J* = 7.4 Hz), 2.49 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.61 (dd, 1 H, *J* = 15.1, 6.6 Hz), 3.25 - 4.0 (m, 9 H), 4.38 (m, 2 H), 4.54 (m, 2 H), 4.65 (m, 2 H), 4.97 (m, 2 H), 5.25 (m, 5 H), 5.88 (m, 1 H), 7.34 (m, 5 H).

(6) To a solution of the compound prepared in (5) above (1.31 g, 1.25 mmol) in THF (20 mL) was added dimethyl malonate (1.0 mL, 0.88 mmol) and the solution was degassed in a stream of argon for 30 min. Tetrakis(triphenylphosphine)palladium(0) (200 mg) was added and the reaction was stirred at room temperature for 2 h, and then concentrated *in vacuo*. The residue obtained was chromatographed on silica gel eluting with 5 -10% EtOAc / $CHCl_3$. The free amine obtained was acylated with (*R*)-3-dodecanoyloxytetradecanoic acid (560 mg, 1.38 mmol) in the presence of EEDQ (370 mg, 1.5 mmol) in CH_2Cl_2 (15 mL). After stirring at room temperature for 18 h, the solvent was removed *in vacuo* and the resultant oil was chromatographed on silica gel eluting with 20 %EtOAc / hexanes to afford 1.02 g (63 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^1H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 78 H), 1.38 (s, 3 H), 1.46 (s, 3 H), 2.26 (m, 4 H), 2.49 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.61 (dd, 1 H, *J* = 15.1, 6.6 Hz), 3.25 - 4.0 (m, 9 H), 5.01 (m, 2 H), 6.02 (d, 1 H, *J* = 8.4 Hz), 7.34 (m, 5 H).

(7) The compound prepared in (6) above (1.0 g, 0.78 mmol) was treated with 90 % aqueous AcOH (20 mL) for 1 h at 60 °C. The solution was concentrated *in vacuo* and residual AcOH and H_2O were removed by azeotroping with toluene (10 mL). The residue was dissolved in CH_2Cl_2, cooled to 0 °C, and treated with pyridine (0.076 mL, 0.94 mmol) and a solution of 2,2,2-trichloro-1,1-dimethylethyl chloroformate (205 mg, 0.86 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was then allowed to warm and stir at room temperature for 18 h. The resulting light yellow solution was treated with diphenyl chlorophosphate (0.24 mL, 1.17 mmol), triethylamine (0.22 mL, 1.56 mmol) and catalytic 4-pyrrolidinopyridine (50 mg), and then stirred an additional 24 h at room temperature. The reaction mixture was diluted with Et_2O (100 mL) and washed with 10 % aq. HCl (50 mL). The organic phase was separated, dried over Na_2SO_4 and concentrated *in vacuo*. Chromatography over silica gel using 10 % EtOAc / hexanes afforded 1.13 g (85 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-

trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, J = 6.9 Hz), 1.1 - 1.6 (m, 78 H), 1.78 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.88 (d, 1 H, J = 6.6 Hz), 2.97 (d, 1 H, J = 6.9 Hz), 3.41 (m, 2 H), 3.72 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, J = 11.8 Hz), 4.64 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, J = 4.3 Hz), 6.05 (d, 1 H, J = 8.4 Hz), 7.23 (m, 15 H).

(8) In the same manner as described in Example 2-(7), the compound prepared in (7) above (1.1 g, 0.65 mmol) was deprotected with zinc (2.1 g, 32 mmol) and acylated with (*R*)-3-dodecanoyloxytetradecanoic acid (330 mg, 0.78 mmol) in the presence of EEDQ (230 mg, 0.94 mmol) to afford 399 mg (37 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-dodecanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(9) In the same manner as described in Example 2-(8), the compound prepared in (8) above (399 mg, 0.24 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 65 mg (16 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 181 - 184° C (dec): IR (film) 3306, 2956, 2922, 2852, 1732, 1644, 1549, 1467, 1377, 1164, 1106, 1051, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.7 Hz), 1.1 - 1.7 (m, 123 H), 2.2 - 2.7 (m, 12 H), 3.06 (q, 6 H, J = 7.1 Hz), 3.3 - 4.0 (m, 13 H), 4.23 (m, 1 H), 4.44 (d, 1 H, J = 7.7 Hz), 5.0 - 5.3 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.9, 173.5, 173.3, 170.8, 170.5, 170.1, 101.0, 75.5, 73.0, 71.1, 70.9, 70.6, 67.9, 61.6, 60.7, 54.4, 50.4, 45.8, 41.6, 41.4, 39.6, 34.6, 31.9, 29.7, 29.4, 29.3, 25.4, 25.1, 22.7, 14.2, 8.6.

Anal. Calcd. for $C_{93}H_{180}N_3O_{18}P \cdot H_2O$: C, 66.59; H, 10.94; N, 2.50; P, 1.85. Found: C, 66.79; H, 10.65; N, 2.36; P, 1.70.

EXAMPLE 5 (B4)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-undecanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_{10}H_{21}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(5), the compound prepared in Example 4-(4) (1.0 g, 1.56 mmol) was acylated with (*R*)-3-undecanoyloxytetradecanoic acid (705 mg, 1.71 mmol) in the presence of EDC·MeI (560 mg, 1.87 mmol) and 4-pyrrolidinopyridine (50 mg) in CH_2Cl_2 (20 mL) to afford 1.23 g (77 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, = 6.9 Hz), 1.1 - 1.6 (m, 36 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.28 (m, 2 H), 2.52 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.61 (dd, 1 H, = 15.5, 6.8 Hz), 3.25 (m, 1 H), 3.35 - 4.0 (m, 9 H), 4.31 (m, 2 H), 4.54 (m, 2 H), 4.64 (m, 2 H), 5.02 (m, 2 H), 5.18 (m, 2 H), 5.25 (m, 1 H), 5.86 (m, 1 H), 7.34 (m, 5 H).

(2) In the same manner as described in Example 4-(6) the compound prepared in (1) above (1.21 g, 1.17 mmol) was deprotected in THF (20 mL) in the presence of dimethyl malonate (1.0 mL, 0.88 mmol) and tetrakis(triphenylphosphine)palladium(0) (200 mg) and then acylated with (*R*)-3-undecanoyloxytetradecanoic acid (540 mg, 1.30 mmol) in the presence of EEDQ (370 mg, 1.5 mmol) to afford 921 mg (61 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-undecanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.6 Hz), 1.1 - 1.7 (m, 72 H), 1.38 (s, 3 H), 1.46 (s, 3 H), 2.26 (m, 3 H), 2.38 (m, 5 H), 2.49 (dd, 1 H, *J*=15.2, 6.0 Hz), 2.61 (dd, 1 H, *J* = 15.0, 6.5 Hz), 3.25 - 4.0 (m, 9 H), 4.30 (m, 2 H), 4.59 (m, 3 H), 6.03 (d, 1 H, *J* = 8.2 Hz), 7.34 (m, 5 H).

(3) In the same manner as described in Example 4-(7) the compound prepared in (2) above (910 g, 0.71 mmol) was deprotected in 90 % aqueous AcOH (20 mL), and then treated with pyridine (0.071 mL, 0.88 mmol) and 2,2,2-trichloro-1,1-dimethylethyl

chloroformate (195 mg, 0.80 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate (0.23 mL, 1.10 mmol), triethylamine (0.20 mL, 1.46 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 1.10 g (89 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-undecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.7 Hz), 1.1 - 1.6 (m, 72 H), 1.78 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.88 (d, 1 H, *J* = 6.7 Hz), 2.97 (d, 1 H, *J* = 6.9 Hz), 3.41 (m, 2 H), 3.72 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, *J* = 11.8 Hz), 4.64 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, *J* = 4.6 Hz), 6.05 (d, 1 H, *J* = 8.4 Hz), 7.22 (m, 15 H).

(4) In the same manner as described in Example 2-(7), the compound prepared in (3) above (1.0 g, 0.59 mmol) was deprotected with zinc (2.0 g, 30 mmol) and acylated with (*R*)-3-undecanoyloxytetradecanoic acid (292 mg, 0.71 mmol) in the presence of EEDQ (210 mg, 0.85 mmol) to afford 388 mg (40 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-undecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(5) In the same manner as described in Example 2-(8), the compound prepared in (4) above (388 mg, 0.24 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 65 mg (17 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-undecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 183-184° C; IR (film) 3306, 2956, 2922, 2852, 1732, 1644, 1550, 1467, 1377, 1164, 1106, 1052, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.8 Hz), 1.1 - 1.7 (m, 117 H), 2.2 - 2.7 (m, 12 H), 3.07 (q, 6 H, *J* = 7.1 Hz), 3.3 - 3.9 (m, 13 H), 4.23 (m, 1 H), 4.45 (d, 1 H, *J* = 8.2 Hz), 5.0 - 5.3 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.8, 173.5, 173.3, 170.8, 170.5, 170.1, 101.0, 75.5, 73.1, 71.5, 71.3, 70.9, 70.6, 67.8, 61.6, 60.7, 54.4, 50.5, 45.8, 41.5, 41.4, 39.5, 34.6, 34.4, 32.0, 31.2, 29.8, 29.7, 29.4, 28.6, 26.1, 25.4, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{90}H_{174}N_3O_{18}P \cdot H_2O$: C, 66.10; H, 10.85; N, 2.57; P, 1.89. Found: C, 66.34; H, 10.69; N, 2.32; P, 1.99.

EXAMPLE 6 (B5)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_9H_{19}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1 R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(5), the compound prepared in Example 4-(4) (2.0 g, 3.12 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (1.36 g, 3.42 mmol) in the presence of EDC·MeI (1.12 g, 3.74 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2 (40 mL) to afford 2.49 g (79 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.7 Hz), 1.1 - 1.6 (m, 34 H), 1.36 (s, 3 H), 1.46 (s, 3 H), 2.27 (t, 2 H, *J* = 6.9 Hz), 2.48 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.60 (dd, 1 H, *J* = 15.1, 6.7 Hz), 3.25 (m, 1 H), 3.35 - 4.0 (m, 9 H), 4.23 (m, 1 H), 4.42 (m, 1 H), 4.52 (m, 4 H), 4.95 (m, 2 H), 5.17 (m, 3 H), 5.88 (m, 1 H), 7.36 (m, 5 H).

(2) In the same manner as described in Example 4-(6) the compound prepared in (1) above (2.47 g, 2.42 mmol) was deprotected in THF (40 mL) in the presence of dimethyl malonate (2.0 mL, 1.75 mmol) and tetrakis(triphenylphosphine)palladium(0) (400 mg) and then acylated with (*R*)-3-decanoyloxytetradecanoic acid (1.06 g, 2.66 mmol) in the presence of EEDQ (740 mg, 3 mmol) to afford 1.86 g (60 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.7 Hz), 1.1 - 1.7 (m, 68 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.32 (m, 4 H), 2.50 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.62 (dd, 1 H, *J* = 15.1, 6.8 Hz), 3.29 (m, 2 H), 3.44 (m, 1 H), 3.55 (m, 1 H), 3.74 (m, 3 H), 3.93 (m, 1 H), 4.18 (m, 1 H), 4.34

(m, 1 H), 4.57 (d, 1 H, J = 11.8 Hz), 4.65 (m, 2 H), 5.01 (m, 2 H), 6.04 (d, 1 H, J = 8.3 Hz), 7.36 (m, 5 H).

(3) In the same manner as described in Example 4-(7) the compound prepared in (2) above (900 mg, 0.72 mmol) was deprotected in 90 % aqueous AcOH (40 mL), and then treated with pyridine (0.071 mL, 0.88 mmol) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (195 mg, 0.80 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate (0.23 mL, 1.10 mmol), triethylamine (0.20 mL, 1.46 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 1.05 g (86 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, J = 6.3 Hz), 1.1 - 1.6 (m, 68 H), 1.78 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.88 (d, 1 H, J = 6.5 Hz), 2.97 (d, 1 H, J = 6.9 Hz), 3.41 (m, 2 H), 3.72 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, J = 11.8 Hz), 4.64 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, J = 4.3 Hz), 6.05 (d, 1 H, J = 8.4 Hz), 7.22 (m, 15 H).

(4) In the same manner as described in Example 2-(7), the compound prepared in (3) above (1.0 g, 0.60 mmol) was deprotected with zinc (2.0 g, 30 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (285 mg, 0.72 mmol) in the presence of EEDQ (210 mg, 0.86 mmol) to afford 332 mg (34 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(5) In the same manner as described in Example 2-(8), the compound prepared in (4) above (332 mg, 0.20 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 173 mg (55 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 179-181° C; IR (film) 3295, 2956, 2923, 2853, 1732, 1650, 1555, 1467, 1377, 1320, 1169, 1134, 1104, 1051,

979, 801, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.9 Hz), 1.1 - 1.7 (m, 114 H), 2.2 - 2.7 (m, 12 H), 3.07 (q, 6 H, J = 6.5 Hz), 3.3 - 4.3 (m, 14 H), 4.45 (d, 1 H, J = 8.0 Hz), 5.0 - 5.3 (m, 4 H), 7.39 (m, 1 H), 7.53 (d, 1 H, J = 9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 173.7, 173.4, 173.2, 170.7, 170.5, 170.1, 101.0, 75.4, 73.1, 71.6, 71.1, 70.8, 70.5, 67.8, 61.4, 60.8, 54.3, 50.4, 45.8, 41.3, 39.5, 34.5, 31.9, 29.8, 29.7, 29.4, 25.4, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{87}H_{168}N_3O_{18}P \cdot H_2O$: C, 65.58; H, 10.75; N, 2.64; P, 1.94. Found: C, 65.49; H, 10.75; N, 2.64; P, 1.97.

EXAMPLE 7 (B6)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-Deoxy-6-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound of R_1=R_2=R_3= *n*-$C_9H_{19}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_8=H, R_6=OH, p=1, R_9=PO_3H_2).

(1) In the same manner as described in Example 4-(7) the compound prepared in Example 6-(2) (900 mg, 0.72 mmol) was deprotected in 90 % aqueous AcOH (20 mL). The residue was dissolved in CH_2Cl_2 (20 mL), cooled to 0 °C, and treated with triethylamine (0.14 mL, 1.0 mmol) and diphenyl chlorophosphate (0.17 mL, 0.8 mmol). The mixture was stirred for an additional 6 h, and then quenched with 50 mL of 10 % HCl. The product was extracted with EtOAc (3 x 50 mL) and dried over Na_2SO_4. Chromatography on silica gel with 50 % EtOAc / hexanes afforded 636 mg (63 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-6-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^1H NMR ($CDCl_3$) δ 0.87 (t, 12 H, J = 6.0 Hz), 1.1 - 1.6 (m, 68 H), 1.79 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.89 (d, 1 H, J = 6.5 Hz), 2.97 (d, 1 H, J = 6.9 Hz), 3.41 (m, 2 H), 3.75 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, J = 11.8 Hz), 4.65 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, J = 4.3 Hz), 6.05 (d, 1 H, J = 8.4 Hz), 7.22 (m, 15 H).

(2) In the same manner as described in Example 2-(7), the compound prepared in (1) above (620 g, 0.44 mmol) was deprotected with zinc (722 mg, 11 mmol)

and acylated with (*R*)-3-decanoyloxytetradecanoic acid (190 mg, 0.48 mmol) in the presence of EEDQ (170 mg, 0.58 mmol) to afford 254 mg (36 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-6-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(3) In the same manner as described in Example 2-(8), the compound prepared in (2) above (254 mg, 0.16 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 34 mg (13 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-6-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 169 - 171° C; IR (film) 3306, 2922, 2853, 1732, 1644, 1548, 1467, 1377, 1316, 1165, 1106, 1053, 856, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.7 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 12 H), 3.05 (m, 6 H), 3.3 - 3.95 (m, 12 H), 4.11 (m, 1 H), 4.34 (m, 1 H), 4.89 (m, 1 H), 5.0 - 5.3 (m, 4 H). ^{13}C NMR ($CDCl_3$) δ 173.8, 173.4, 171.1, 170.5, 101.3, 75.3, 74.9, 71.2, 71.0, 70.6, 68.8, 67.3, 65.1, 61.4, 53.4, 50.7, 45.9, 41.5, 41.3, 39.6, 34.6, 32.0, 29.8, 29.6, 29.4, 25.3, 25.1, 22.7, 14.1, 8.7.

Anal. Calcd. for $C_{87}H_{168}N_3O_{18}P \cdot H_2O$: C, 65.58; H, 10.75; N, 2.64; P, 1.94. Found: C, 65.60; H, 10.34; N, 2.36; P, 2.01..

EXAMPLE 8 (B7)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-nonanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_8H_{17}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(5), the compound prepared in Example 4-(4) (1.0 g, 1.56 mmol) was acylated with (*R*)-3-nonanoyloxytetradecanoic acid (660 mg, 1.71 mmol) in the presence of EDC MeI (560 mg, 1.87 mmol) and 4-pyrrolidinopyridine (50 mg) in CH_2Cl_2 (20 mL) to afford 1.31 g (83 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-

isopropylidene-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 6 H, *J* = 6.8 Hz), 1.1 - 1.6 (m, 32 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.27 (t, 2 H, *J* = 7.4 Hz), 2.50 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.63 (dd, 1 H, *J* = 15.1, 6.8 Hz), 3.26 (m, 1 H), 3.35 - 4.0 (m, 9 H), 4.32 (d, 1 H, *J* = 7.8 Hz), 4.41 (d, 1 H, *J* = 12.0 Hz), 4.51 (m, 4 H), 4.95 (m, 2 H), 5.18 (m, 2 H), 5.29 (d, 1 H, *J* = 17.2 Hz), 5.88 (m, 1 H), 7.36 (m, 5 H).

(2) In the same manner as described in Example 4-(6) the compound prepared in (1) above (1.29 g, 1.28 mmol) was deprotected in THF (20 mL) in the presence of dimethyl malonate (1.0 mL, 0.88 mmol) and tetrakis(triphenylphosphine)palladium(0) (200 mg) and then acylated with (*R*)-3-nonanoyloxytetradecanoic acid (540 mg, 1.41 mmol) in the presence of EEDQ (370 mg, 1.5 mmol) to afford 1.02 g (65 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-nonanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.1 Hz), 1.1 - 1.7 (m, 64 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.28 (m, 4 H), 2.50 (dd, 1 H, *J* = 15.5, 6.0 Hz), 2.62 (dd, 1 H, *J* = 14.8, 6.3 Hz), 3.27 (m, 2 H), 3.44 (m, 1 H), 3.55 (m, 1 H), 3.74 (m, 3 H), 3.93 (m, 1 H), 4.18 (m, 1 H), 4.34 (m, 2 H), 4.57 (d, 1 H, *J* = 11.8 Hz), 4.65 (m, 2 H), 4.97 (t, 1 H, *J* = 9.6 Hz), 5.06 (d, 1 H, *J* = 8.6 Hz), 5.15 (m, 2 H), 6.05 (d, 1 H, *J* = 8.2 Hz), 7.35 (m, 5 H).

(3) In the same manner as described in Example 4-(7) the compound prepared in (2) above (1.0 g, 0.81 mmol) was deprotected in 90 % aqueous AcOH (20 mL), treated with pyridine (0.080 mL, 0.98 mmol) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (215 mg, 0.89 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate (0.25 mL, 1.22 mmol), triethylamine (0.21 mL, 1.52 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 1.17 g (87 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-nonanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.1 Hz), 1.1 - 1.6 (m, 64 H), 1.78 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.88 (d, 1 H, *J* = 6.5

Hz), 2.97 (d, 1 H, J = 6.9 Hz), 3.41 (m, 2 H), 3.72 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, J = 11.8 Hz), 4.64 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, J = 4.3 Hz), 6.05 (d, 1 H, J = 8.4 Hz), 7.22 (m, 15 H).

(4) In the same manner as described in Example 2-(7), the compound prepared in (3) above (1.1 g, 0.66 mmol) was deprotected with zinc (2.2 g, 33 mmol) and acylated with (*R*)-3-nonanoyloxytetradecanoic acid (305 mg, 0.79 mmol) in the presence of EEDQ (235 mg, 0.95 mmol) to afford 373 mg (35 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-nonanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(5) In the same manner as described in Example 2-(8), the compound prepared in (4) above (373 mg, 0.23 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 43 mg (12 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-nonanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 176-179° C; IR (film) 3298, 2956, 2923, 2853, 1733, 1646, 1551, 1467, 1337, 1316, 1254, 1166, 1106, 1053, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.87 (t, 18 H, J = 6.7 Hz), 1.1 - 1.7 (m, 105 H), 2.2 - 2.7 (m, 12 H), 3.03 (q, 6 H, J = 7.0 Hz), 3.3 - 4.3 (m, 14 H), 4.43 (d, 1 H, J = 7.1 Hz), 5.0 - 5.3 (m, 4 H), 7.12 (d, 1 H, J = 7.7 Hz), 7.17 (d, 1 H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$) δ 173.9, 173.5, 173.3, 170.8, 170.5, 170.1, 100.9, 75.5, 73.1, 71.4, 71.1, 70.9, 70.6, 67.8, 61.6, 60.7, 54.3, 50.5, 45.8, 41.6, 41.4, 39.5, 34.6, 34.4, 32.0, 31.9, 29.8, 29.4, 29.3, 25.4, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{88}H_{164}N_3O_{18}P$: C, 65.81; H, 10.65; N, 2.74; P, 2.02. Found: C, 66.14; H, 10.46; N, 2.58; P, 1.84.

EXAMPLE 9 (B8)

Preparation of 3-Hydroxy-(*S*)-2-[(*R*)-3-heptanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_6H_{13}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=1, R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(5), the compound prepared in Example 4-(4) (1.0 g, 1.56 mmol) was acylated with (*R*)-3-heptanoyloxytetradecanoic acid (610 mg, 1.71 mmol) in the presence of EDC MeI (560 mg, 1.87 mmol) and 4-pyrrolidinopyridine (50 mg) in CH_2Cl_2 (20 mL) to afford 1.24 g (82 %) of 3-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.0 Hz), 1.1 - 1.6 (m, 28 H), 1.38 (s, 3 H), 1.47 (s, 3 H), 2.29 (t, 2 H, *J* = 7.4 Hz), 2.51 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.63 (dd, 1 H, *J* = 15.1, 6.8 Hz), 3.26 (m, 1 H), 3.35 - 4.0 (m, 9 H), 4.32 (d, 1 H, *J* = 7.3 Hz), 4.41 (d, 1 H, *J* = 12.0 Hz), 4.51 (m, 4 H), 4.95 (m, 2 H), 5.18 (m, 2 H), 5.29 (d, 1 H, *J* = 17.3 Hz), 5.88 (m, 1 H), 7.36 (m, 5 H).

(2) In the same manner as described in Example 4-(6) the compound prepared in (1) above (1.22 g, 1.25 mmol) was deprotected in THF (20 mL) in the presence of dimethyl malonate (1.0 mL, 0.88 mmol) and tetrakis(triphenylphosphine)palladium(0) (200 mg) and then acylated with (*R*)-3-heptanoyloxytetradecanoic acid (490 mg, 1.38 mmol) in the presence of EEDQ (370 mg, 1.5 mmol) to afford 925 mg (62 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-heptanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.7 Hz), 1.1 - 1.7 (m, 56 H), 1.37 (s, 3 H), 1.46 (s, 3 H), 2.32 (m, 4 H), 2.50 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.62 (dd, 1 H, *J* = 15.1, 6.8 Hz), 3.29 (m, 2 H), 3.44 (m, 1 H), 3.55 (m, 1 H), 3.74 (m, 3 H), 3.93 (m, 1 H), 4.18 (m, 1 H), 4.34 (m, 1 H), 4.57 (d, 1 H, *J* = 11.8 Hz), 4.65 (m, 2 H), 5.01 (m, 2 H), 6.04 (d, 1 H, *J* = 8.3 Hz), 7.36 (m, 5 H).

(3) In the same manner as described in Example 4-(7) the compound prepared in (2) above (920 mg, 0.76 mmol) was deprotected in 90 % aqueous AcOH (20 mL), and then treated with pyridine (0.075 mL, 0.92 mmol) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (200 mg, 0.84 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate(0.24 mL, 1.14 mmol), triethylamine (0.21 mL, 1.52 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 1.03 g (83 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-heptanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-heptanoyloxytctradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.3 Hz), 1.1 - 1.6 (m, 56 H), 1.78 (s, 3 H), 1.86 (s, 3 H), 2.01 (m, 1 H), 2.18 (m, 3 H), 2.40 (m, 2 H), 2.67 (m, 1 H), 2.88 (d, 1 H, *J* = 6.5 Hz), 2.97 (d, 1 H, *J* = 6.9 Hz), 3.41 (m, 2 H), 3.72 (m, 1 H), 3.82 (m, 1 H), 4.24 (m, 1 H), 4.42 (d, 1 H, *J* = 11.8 Hz), 4.64 (m, 3 H), 5.16 (m, 1 H), 5.39 (m, 2 H), 5.75 (d, 1 H, *J* = 4.3 Hz), 6.05 (d, 1 H, *J* = 8.4 Hz), 7.22 (m, 15 H).

(4) In the same manner as described in Example 2-(7), the compound prepared in (3) above (1.0 g, 0.61 mmol) was deprotected with zinc (2.0 g, 31 mmol) and acylated with (*R*)-3-heptanoyloxytetradecanoic acid (260 mg, 0.73 mmol) in the presence of EEDQ (220 mg, 0.88 mmol) to afford 203 mg (21 %) of 3-benzyloxy-(*S*)-2-[(*R*)-3-heptanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(5) In the same manner as described in Example 2-(8), the compound prepared in (4) above (203 mg, 0.13 mmol) was hydrogenated in the presence of palladium hydroxide (100 mg) on carbon in EtOH (10 mL) and platinum oxide (200 mg) in EtOH / AcOH (10:1) to afford 39 mg (21 %) of 3-hydroxy-(*S*)-2-[(*R*)-3-heptanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 171-172° C; IR (film) 3305, 2955, 2924, 2853, 1734, 1644, 1553, 1466, 1377, 1170, 1102, 1052, 722 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (m, 18 H), 1.1 - 1.7 (m, 93 H), 2.2 - 2.7 (m, 12 H), 3.06 (q, 6 H, *J* = 7.1 Hz), 3.3 - 4.0 (m, 13 H), 4.23 (q, 1 H, *J* = 9.3 Hz), 4.43 (d, 1 H, *J* = 8.2

Hz), 5.0 - 5.3 (m, 4 H), 7.30 (d, 1 H, J = 8.5 Hz), 7.43 (d, 1 H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 173.8, 173.5, 173.2, 170.8, 170.5, 170.2, 101.0, 77.2, 75.5, 73.1, 71.6, 71.1, 70.9, 70.6, 67.8, 61.6, 60.8, 54.4, 50.5, 45.8, 41.6, 41.4, 39.5, 34.6, 34.4, 32.0, 31.6, 29.8, 29.6, 29.4, 28.9, 25.4, 25.1, 22.7, 22.6, 14.1, 8.6.

Anal. Calcd. for $C_{78}H_{150}N_3O_{18}P \cdot H_2O$: C, 63.86; H, 10.44; N, 2.86; P, 2.11. Found: C, 63.47; H, 10.20; N, 2.59; P, 2.02.

EXAMPLE 10 (B9)

Preparation of 4-Hydroxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=p=1, m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(3) the compound prepared in Example 4-(1) (3.1 g, 5.9 mmol) and (*R*)-3-(allyloxycarbonylamino)-4-benzyloxy-1-butanol (1.1 g, 3.94 mmol) were coupled in the presence of boron trifluoride etherate (3.0 mL, 23.6 mmol) to afford 1.96 g (67 %) of 4-benzyloxy-(*S*)-3-(allyloxycarbonylamino)butyl 2-deoxy-3,4,6-tri-*O*-acetyl-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid. In the same manner as described in Example 4-(4) the compound prepared above (1.8 g, 2.43 mmol) was deacylated in methanol (25 mL) with ammonium hydroxide (5 mL) and then treated with 2,2-dimethoxypropane (25 mL) and camphorsulfonic acid (100 mg) to afford 1.34 g (84 %) of 4-benzyloxy-(*S*)-3-(allyloxycarbonylamino)butyl 2-deoxy-4,6-*O*-isopropylidine-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside.

(2) In the same manner as described in Example 4-(5), the compound prepared in (1) above (1.0 g, 1.53 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (670 mg, 1.68 mmol) in the presence of EDC·MeI (550 mg, 1.85 mmol) and 4-pyrrolidinopyridine (50 mg) in CH_2Cl_2 (15 mL) to afford 1.03 g (65 %) of 4-benzyloxy-(*S*)-3-(allyloxycarbonylamino)butyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.9 Hz), 1.1 - 1.6 (m, 34 H), 1.37 (s, 3 H), 1.47 (s, 3 H), 1.85 (m, 2 H), 2.28 (t, 2 H, J = 7.6 Hz), 2.50 (dd, 1 H, J = 15.1, 6.0 Hz), 2.63 (dd, 1 H, J =

15.1, 6.7 Hz), 3.30 (m, 1 H), 3.49 (m, 4 H), 3.68 (t, 1 H, *J* = 9.4 Hz), 3.77 (t, 1 H, *J* = 10.4 Hz), 3.92 (m, 3 H), 4.54 (m, 5 H), 4.69 (m, 2 H), 5.1 - 5.4 (m, 4 H), 5.91 (m, 1 H), 7.33 (m, 5 H).

(3) In the same manner as described in Example 4-(6) the compound prepared in (2) above (1.0 g, 0.97 mmol) was deprotected in THF (20 mL) in the presence of dimethyl malonate (1.0 mL, 0.88 mmol) and tetrakis(triphenylphosphine)palladium(0) (200 mg) and then acylated with (*R*)-3-decanoyloxytetradecanoic acid (425 mg, 1.07 mmol) in the presence of EEDQ (317 mg, 1.28 mmol) to afford 660 mg (51 %) of 4-benzyloxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.6 Hz), 1.1 - 1.7 (m, 68 H), 1.37 (s, 3 H), 1.47 (s, 3 H), 2.26 (q, 2 H, *J* = 7.1 Hz), 2.41 (m, 2 H), 2.62 (dd, 1 H, *J* = 14.9, 6.4 Hz), 3.29 (m, 1 H), 3.48 (m, 3 H), 3.71 (m, 2 H), 3.92 (m, 2 H), 4.18 (m, 1 H), 4.49 (m, 2 H), 4.68 (q, 2 H, *J* = 11.5 Hz), 5.15 (m, 2 H), 5.55 (d, 1 H, *J* = 8.8 Hz), 6.17 (d, 1 H, *J* = 7.2 Hz), 7.32 (m, 5 H).

(4) In the same manner as described in Example 4-(7) the compound prepared in (3) above (640 mg, 0.48 mmol) was deprotected in 90 % aqueous AcOH (20 mL), and then treated with pyridine (0.047 mL, 0.58 mmol) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (127 mg, 0.53 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate (0.15 mL, 0.72 mmol), triethylamine (0.13 mL, 0.96 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 389 mg (47 %) of 4-benzyloxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.6 Hz), 1.1 - 1.6 (m, 68 H), 1.79 (s, 3 H), 1.86 (s, 3 H), 2.22 (m, 4 H), 2.40 (m, 4 H), 3.49 (m, 4 H), 3.78 (m, 1 H), 3.93 (m, 1 H), 4.1 - 4.5 (m, 5 H), 4.9 - 4.6 (m, 4 H), 5.13 (m, 2 H), 5.51 (t, 1 H, *J* = 8.9 Hz), 5.84 (d, 1 H, *J* = 6.9 Hz), 6.09 (d, 1 H, *J* = 8.0 Hz), 7.26 (m, 15 H).

(5) In the same manner as described in Example 2-(7), the compound prepared in (4) above (375 g, 0.23 mmol) was deprotected with zinc (752 mg, 11.5

mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (101 mg, 0.25 mmol) in the presence of EEDQ (70 mg, 0.28 mmol) to afford 270 mg (67 %) of 4-benzyloxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(6) In the same manner as described in Example 2-(8), the compound prepared in (5) above (270 mg, 0.15 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 93 mg (39 %) of 4-hydroxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 179-181° C (dec): IR (film) 3287, 2956, 2923, 2853, 1734, 1654, 1552, 1466, 1378, 1246, 1164, 1106, 1085, 1052, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 14 H), 3.06 (q, 6 H, *J* = 6.9 Hz), 3.2 - 4.0 (m, 13 H), 4.21 (m, 1 H), 4.50 (d, 1 H, *J* = 7.7 Hz), 5.0 - 5.3 (m, 4 H), 7.11 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.8, 173.5, 173.3, 170.9, 170.5, 170.1, 101.1, 77.2, 75.5, 72.8, 71.3, 71.0, 70.6, 66.4, 64.0, 60.7, 54.8, 50.2, 45.8, 41.6, 39.5, 34.6, 34.5, 34.4, 32.0, 30.6, 29.8, 29.7, 29.6, 29.5, 29.4, 25.4, 25.1, 22.7, 14.2, 8.6.

Anal. Calcd. for $C_{88}H_{170}N_3O_{18}P$: C, 66.65; H, 10.78; N, 2.64; P, 1.95. Found: C, 66.65; H, 10.68; N, 2.50; P, 1.94.

EXAMPLE 11 (B10)

Preparation of 4-Hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=m=q=0, R_4=R_5=R_7=R_9=H, R_6=OH, p=2, R_8=PO_3H_2).

(1) In the same manner as described in Example 4-(3) the compound prepared in Example 4-(1) (5.1 g, 9.7 mmol) and (*R*)-2-(allyloxycarbonylamino)-4-benzyloxy-1-butanol (1.8 g, 6.45 mmol) were coupled in the presence of boron trifluoride etherate (4.9 mL, 38.0 mmol) to afford 2.92 g (61 %) of 4-benzyloxy-(*S*)-2-(allyloxycarbonylamino)propyl 2-deoxy-3,4,6-tri-O-acetyl-2-(2,2,2-

trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid. In the same manner as described in Example 4-(4) the compound prepared above (2.6 g, 3.51 mmol) was deacylated in methanol (35 mL) with ammonium hydroxide (7 mL) and then treated with 2,2-dimethoxypropane (35 mL) and camphorsulfonic acid (100 mg) to afford 1.9 g (72 %) of 4-benzyloxy-(*S*)-2-(allyloxycarbonylamino)butyl 2-dcoxy-4,6-*O*-isopropylidine-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside.

(2) In the same manner as described in Example 4-(5), the compound prepared in (1) above (1.0 g, 1.53 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (670 mg, 1.68 mmol) in the presence of EDCMeI (550 mg, 1.85 mmol) and 4-pyrrolidinopyridine (50 mg) in CH_2Cl_2 (15 mL) to afford 1.28 g (81 %) of 4-benzyloxy-(*S*)-2-(allyloxycarbonylamino)butyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 34 H), 1.37 (s, 3 H), 1.47 (s, 3 H), 1.82 (m, 2 H), 2.28 (t, 2 H, *J* = 7.7 Hz), 2.50 (dd, 1 H, *J* = 15.3, 6.0 Hz), 2.63 (dd, 1 H, *J* = 15.2, 6.7 Hz), 3.16 (m, 1 H), 3.56 (m, 3 H), 3.65 (t, 1 H, *J* = 9.6 Hz), 3.75 (t, 1 H, *J* = 10.4 Hz), 3.88 (m, 4 H), 4.32 (d, 1 H, *J* = 8.5 Hz), 4.46 (s, 2 H), 4.54 (m, 2 H), 4.67 (m, 2 H), 4.90 (m, 1 H), 5.26 (m, 3 H), 5.89 (m, 1 H), 7.33 (m, 5 H).

(3) In the same manner as described in Example 4-(6) the compound prepared in (2) above (1.25 g, 1.21 mmol) was deprotected in THF (20 mL) in the presence of dimethyl malonate (1.0 mL, 0.88 mmol) and tetrakis(triphenylphosphine)palladium(0) (200 mg) and then acylated with (*R*)-3-decanoyloxytetradecanoic acid (530 mg, 1.33 mmol) in the presence of EEDQ (362 mg, 1.46 mmol) to afford 1.16 g (72 %) of 4-benzyloxy-(*S*)-3-[(*R*)-3-decanoyloxytetradecanoylamino]propyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.4 Hz), 1.1 - 1.7 (m, 68 H), 1.37 (s, 3 H), 1.45 (s, 3 H), 2.26 (q, 2 H, *J* = 7.4 Hz), 2.34 (m, 1 H), 2.50 (dd, 1 H, *J* = 15.1, 6.0 Hz), 2.62 (dd, 1 H, *J* = 15.4, 6.3 Hz), 3.12 (m, 1 H), 3.5 - 3.95 (m, 7 H), 4.14 (m, 1 H), 4.29 (d, 1 H, *J* = 8.0 Hz), 4.67 (m, 2 H), 4.86 (t, 1 H, *J* = 9.6 Hz),5.15 (m, 2 H), 6.16 (d, 1 H, *J* = 8.3 Hz), 7.35 (m, 5 H).

(4) In the same manner as described in Example 4-(7) the compound prepared in (3) above (1.1 g, 0.83 mmol) was deprotected in 90 % aqueous AcOH (20 mL), and then treated with pyridine (0.080 mL, 1.0 mmol) and 2,2,2-trichloro-1,1-dimethylethyl chloroformate (220 mg, 0.91 mmol) in CH_2Cl_2 followed by diphenyl chlorophosphate (0.26 mL, 1.25 mmol), triethylamine (0.23 mL, 1.66 mmol) and catalytic 4-pyrrolidinopyridine (50 mg) to afford 802 mg (56 %) of 4-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 12 H, *J* = 6.8 Hz), 1.1 - 1.6 (m, 68 H), 1.79 (s, 3 H), 1.88 (s, 3 H), 2.23 (m, 4 H), 2.37 (m, 4 H), 3.57 (m, 4 H), 3.83 (m, 1 H), 4.29 (m, 3 H), 4.44 (m, 2 H), 4.69 (m, 4 H), 5.14 (m, 4 H), 5.62 (d, 1 H, *J* = 7.6 Hz), 6.15 (d, 1 H, *J* = 8.3 Hz), 7.25 (m, 15 H).

(5) In the same manner as described in Example 2-(7), the compound prepared in (4) above (750 mg, 0.43 mmol) was deprotected with zinc (1.42 g, 21.7 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (190 mg, 0.48 mmol) in the presence of EEDQ (130 mg, 0.53 mmol) to afford 483 mg (64 %) of 4-benzyloxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside as a colorless amorphous solid.

(6) In the same manner as described in Example 2-(8), the compound prepared in (5) above (483 mg, 0.27 mmol) was hydrogenated in the presence of palladium hydroxide (150 mg) on carbon in EtOH (10 mL) and platinum oxide (300 mg) in EtOH / AcOH (10:1) to afford 238 mg (55 %) of 4-hydroxy-(*S*)-2-[(*R*)-3-decanoyloxytetradecanoyl]butyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyltetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 181-183° C (dec): IR (film) 3294, 2956, 2923, 2853, 1732, 1650, 1556, 1466, 1377, 1320, 1246, 1172, 1108, 1082, 1058, 859, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 14 H), 3.06 (q, 6 H, *J* = 7.1 Hz), 3.2 - 4.0 (m, 13 H), 4.21 (m, 1 H), 4.46 (d, 1 H, *J* = 8.3 Hz), 5.0 - 5.3 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.9, 173.4,

173.2, 171.2, 170.7, 101.0, 77.2, 75.4, 73.1, 71.4, 71.3, 71.1, 70.9, 70.6, 60.7, 58.4, 54.7, 46.3, 45.9, 41.6, 41.1, 39.7, 34.8, 34.6, 34.4, 31.9, 29.8, 29.6, 29.5, 29.3, 25.4, 25.3, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{88}H_{170}N_3O_{18}P$: C, 66.51; H, 10.78; N, 2.64; P, 1.95. Found: C, 66.81; H, 10.68; N, 2.53; P, 1.79.

EXAMPLE 12 (B11)

Preparation of *N*-[(*R*)-3-Tetradecanoyloxytetradecanoyl]-*O*-[2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt (Compound (I), $R_1=R_2=R_3=n\text{-}C_{13}H_{27}CO$, X=Y=O, n=m=p=q=0, $R_4=R_5=R_7=R_9=H$, $R_6=CO_2H$, $R_8=PO_3H_2$).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (0.212 g, 1.08 mmol) was acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.541 g, 1.19 mmol) in the presence of EDC·MeI (0.353 g, 1.19 mmol) to give 0.642 g (94%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-L-serine benzyl ester as a waxy solid: mp 56-61°C; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J*= ~7 Hz), 1.1-1.7 (m, 42 H), 2.29 (t, 2 H, *J*=7.5 Hz), 2.50 (m, 2 H), 3.87 (br t, 1 H), 3.95 (m, 2 H), 4.65 (m, 1 H), 5.1-5.25 (m, 3 H), 6.69 (d, 1 H, *J*=7 Hz), 7.34 (br s, 5 H).

(2) In the same manner as described in Example 2-(6), the compound prepared in (1) above (0.19 g, 0.30 mmol) and the compound prepared in Example 2-(4) (0.635 g, 0.478 mmol) were coupled in the presence of mercury cyanide (0.3 g , 1.2 mmol) to give 0.425 g (77%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (0.405 g, 0.22 mmol) was deprotected with zinc (0.72 g, 11 mmol) and acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.12 g, 0.26 mmol) in the presence of EEDQ (0.082 g, 0.33 mmol) to give 0.277 g (66%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88

(t, 18 H, *J*= ~6.5 Hz) 1.0-1.75 (m, 126 H), 2.15-2.45 (m, 10 H), 2.53 (dd, 1 H, *J*=14.7, 6.0 Hz), 2.67 (dd, 1 H, *J*=14, 6.0 Hz), 3.25 (br t, 1 H, *J*=7 Hz), 3.35-3.75 (m, 4 H), 3.88 (dd, 1 H, *J*=11.1 Hz), 4.23 dd, 1 H, *J*=11.1, 3 Hz), 4.6-4.75 (m, 2 H), 5.03 (d, 1 H, *J*=8.1 Hz), 5.05-5.25 (m, 4 H), 5.48 (t, 1 H, *J*= ~10 Hz), 6.40 (d, 1 H, *J*=7.5 Hz), 7.01 (d, 1 H, *J*=8.1 Hz), 7.1-7.4 (m, 15 H).

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (0.253 g, 0.133 mmol) was hydrogenated in the presence of 5% palladium on carbon (50 mg) and platinum oxide (120 mg) to give 0.155 g (62%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a colorless solid: mp 180°C (dec); IR (film) 3322, 2956, 2924, 2852, 1736, 1732, 1681, 1673, 1667, 1660, 1651, 1467, 1456, 1247, 1174, 1110, 1081 cm^{-1}; ^1H NMR ($CDCl_3$-CD_3OD) δ 0.88 (t, 18 H, *J*= ~7 Hz), 1.0-1.7 (m, 135 H), 2.2-2.75 (m, 12 H), 3.05 (q, 6 H, *J*=7 Hz), 3.30 (br s, 13 H), 3.7-3.9 (m, 3 H), 3.96 (d, 1 H, *J*=12 Hz), 4.05-4.3 (m, 2 H), 4.34 (m, 1 H), 4.53 (d, 1 H, *J*=7.8 Hz), 5.05-5.3 (m, 4 H), 7.25-7.35 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 173.2, 171.0, 170.3, 170.2, 169.9, 169.8, 100.8, 75.1, 73.4, 71.1, 70.7, 70.4, 70.3, 60.2, 54.3, 45.6, 41.2, 41.1, 39.2, 34.6, 34.4, 34.2, 32.0, 29.8, 29.5, 25.4, 25.2, 22.7, 14.2, 8.6.

Anal. Calcd for $C_{90}H_{190}N_3O_{19}P \cdot 5\ H_2O$: C, 64.35; H, 10.91; N, 2.27; P, 1.68. Found: C, 64.16; H, 10.92; N, 2.37; P, 1.91.

EXAMPLE 13 (B12)

Preparation of *N*-[(*R*)-3-Dodecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{11}H_{23}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-dodecanoyloxytetradecanoic acid (935 mg, 2.2 mmol) in the presence of EDC·MeI (745 mg, 2.5 mmol) in CH_2Cl_2 to afford 1.08 g (90 %) of *N*-[(*R*)-3-dodecanoyloxytetradecanoyl]-L-serine benzyl ester: mp 53-54 °C. ^1H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J*= 6.5 Hz), 1.1 - 1.6 (m, 46 H), 2.30 (t, 2 H, *J*= 7.7 Hz),

2.50 (d, 2 H, 5.6 Hz), 2.62 (t, 1 H, J = 6.2 Hz), 3.97 (m, 2 H), 4.65 (m, 1 H), 5.19 (m, 3 H), 6.63 (d, 1 H, J = 6.8 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-dodecanoyloxytetradecanoic acid (946 mg, 2.22 mmol) in the presence of EDC MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in aqueous AcOH (25 mL) to afford 1.30g (81 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8 H), 1.25 (m, 28 H), 1.59 (m, 4 H), 2.30 (t, 2 H, J = 7.5 Hz), 2.52 (m, 2 H), 3.42 (m, 1 H), 3.55 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, J = 11.8, 4.6 Hz), 3.94 (m, 2 H), 4.57 (d, 1 H, J = 8.2 Hz), 4.71 (m, 2 H), 5.07 (m, 2 H), 5.27 (d, 1 H, J = 8.8 Hz).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.30 g, 1.51 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (398 mg, 1.66 mmol) and pyridine (0.15 mL, 1.83 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.42 mL, 3.02 mmol), diphenyl chlorophosphate (0.47 mL, 2.27 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.39 g (71 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 8 H), 1.1 - 1.7 (m, 46 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.23 (m, 6 H), 3.34 (m, 1 H), 3.59 (m, 1 H), 3.80 (m, 1 H), 3.96 (m, 1 H), 4.32 (m, 2 H), 4.63 (m, 2 H), 4.83 (d, 1 H, J = 11.9 Hz), 5.02 (d, 1 H, J = 8.2 Hz), 5.20 (m, 1 H), 5.65 (m, 2 H), 7.29 (m, 10 H).

(4) The compound prepared in (3) above (1.30 g, 1.0 mmol) in CH_2Cl_2 (15 mL) was treated at 0 °C with TFA (5 mL) and then allowed to warm to room temperature for 18 h. The solvent was removed in vacuo and the remaining TFA was removed by azeotroping with toluene. The lactol was treated with the Vilsmeier reagent prepared from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The reaction was allowed to warm slowly to room temperature overnight and was partitioned between 50 mL of saturated aqueous $NaHCO_3$ and ether (50 mL).

The layers were separated and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography on silica gel with 10 % EtOAc / hexanes afforded 1.09 g (90 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.8 Hz), 1.2 - 1.70 (m, 46 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, *J* = 7.7 Hz), 2.43 (m, 2 H), 4.30 (m, 4 H), 4.72 (m, 3 H), 5.09 (m, 1 H), 5.50 (t, 1 H, *J* = 9.5 Hz), 5.79 (d, 1 H, *J* = 8.0 Hz), 6.27 (d, 1 H, *J* = 3.6 Hz), 7.19 (m, 10 H).

(5) To a solution of compounds prepared in (1) and (4) (540 mg, 0.90 mmol, and 1.0 g, 0.82 mmol, respectively) in 1,2-dichloroethane (20 mL), powdered 4A molecular sieves (300 mg) were added and the suspension was stirred for 30 min. AgOTf (1.16 g, 4.5 mmol) was added in one portion, after 30 min the slurry was filtered through silica gel and eluted with 30 % EtOAc / hexanes to afford 1.10 g (75 %) of *N*-[(*R*)-3-dodecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.5 Hz), 1.1 - 1.65 (m, 92 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.1 - 2.5 (m, 8 H), 3.67 (m, 2 H), 4.30 (m, 3 H), 4.72 (m, 5 H), 5.18 (m, 4 H), 5.46 (m, 1 H), 6.07 (m, 1 H), 6.62 (d, 1 H, *J* = 7.9 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (1.0 g, 0.56 mmol) was deprotected with zinc (1.83 g, 28 mmol) and acylated with (*R*)-3-dodecanoyloxytetradecanoic acid (285 mg, 0.67 mmol) in the presence of EEDQ (185 mg, 0.74 mmol) to afford 420 mg (44 %) of *N*-[(*R*)-3-dodecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-dodecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (420 mg, 0.24 mmol) was hydrogenated in the presence of palladium hydroxide on carbon in EtOH (10 mL) and platinum oxide (400 mg) in EtOH / AcOH (10:1) to afford 240 mg (60 %) of *N*-[(*R*)-3-dodecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-dodecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-

dodecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 181-182° C; IR (film) 3289, 2956, 2920, 2851, 1731, 1656, 1557, 1467, 1378, 1182, 1108, 1080, 1052, 852, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.7 Hz), 1.1 - 1.7 (m, 123 H), 2.2 - 2.7 (m, 12 H), 3.06 (q, 6 H, J = 7.2 Hz), 3.35 (m, 1 H), 3.70 (m, 6 H), 3.88 (m, 2 H), 4.20 (m, 1 H), 4.56 (d, 1 H, J = 8.1 Hz), 4.59 (br s, 1 H), 5.16 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 176.9, 173.3, 173.2, 172.7, 169.6, 169.1, 101.5, 74.8, 71.2, 70.9, 69.2, 60.5, 53.1, 51.4, 46.1, 41.5, 41.0, 39.2, 34.3, 34.2, 34.0, 32.0, 29.8, 29.7, 29.4, 29.2, 25.6, 25.3, 25.2, 25.1, 22.7, 14.1, 8.7.

Anal. Calcd. for $C_{93}H_{178}N_3O_{19}P \cdot H_2O$: C, 66.04; H, 10.73; N, 2.48; P, 1.83. Found: C, 66.04; H, 10.73; N, 2.48; P, 1.86.

EXAMPLE 14 (B13)

Preparation of *N*-[(*R*)-3-Undecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{10}H_{21}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-undecanoyloxytetradecanoic acid (905 mg, 2.2 mmol) in the presence of EDC·MeI (745 mg, 2.5 mmol) in CH_2Cl_2 to afford 1.08 g (92 %) of *N*-[(*R*)-3-undecanoyloxytetradecanoyl]-L-serine benzyl ester: mp 53-54 °C; ^1H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.9 Hz), 1.1 - 1.7 (m, 44 H), 2.30 (t, 2 H, J = 7.7 Hz), 2.49 (d, 2 H, J = 5.8 Hz), 3.99 (m, 2 H), 4.65 (m, 1 H), 5.19 (m, 3 H), 6.58 (d, 1 H, J = 6.9 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-undecanoyloxytetradecanoic acid (915 mg, 2.22 mmol) in the presence of EDC·MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in aqueous AcOH (25 mL) to afford 1.41 g (82 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8 H), 1.25 (m, 32 H), 1.60 (m, 4 H), 2.31 (t, 2 H, J = 7.5 Hz), 2.52 (m, 2 H), 3.42 (m, 1 H),

3.55 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, J = 11.8, 4.6 Hz), 3.94 (m, 2 H), 4.57 (d, 1 H, J = 8.2 Hz), 4.71 (m, 2 H), 5.07 (m, 2 H), 5.27 (d, 1 H, J = 8.7 Hz).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.30, 1.53 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (403 mg, 1.68 mmol) and pyridine (0.15 mL, 1.85 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.43 mL, 3.06 mmol), diphenyl chlorophosphate (0.48 mL, 2.30 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.37 g (70 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphcnylphosphono-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 8 H), 1.1 - 1.7 (m, 44 H), 1.80 (s, 3 H), 1.89 (s, 3 H), 2.23 (m, 6 H), 3.58 (m, 3 H), 4.32 (m, 1 H), 4.71 (m, 2 H), 4.83 (d, 1 H, J = 12.1 Hz), 5.01 (d, 1 H, J = 8.1 Hz), 5.20 (m, 1 H), 5.62 (m, 2 H), 7.25 (m, 10 H).

(4) In the same manner as described in Example 13-(4), the compound prepared in (4) above (1.28 g, 1.0 mmol) was deprotected with TFA (5 mL) and then treated with the Vilsmeier reagent generated from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) to give 1.12 g (93 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.7 Hz), 1.1 - 1.55 (m, 44 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (m, 2 H), 2.43 (m, 2 H), 4.34 (m, 4 H), 4.72 (m, 3 H), 5.09 (m, 1 H), 5.50 (t, 1 H, J = 9.6 Hz), 5.80 (d, 1 H, J = 8.0 Hz), 6.26 (d, 1 H, J = 3.4 Hz), 7.26 (m, 10 H).

(5) In the same manner as described in Example 13-(5), compounds prepared in (1) and (4) above (530 mg, 0.90 mmol, and 1.0 g, 0.83 mmol, respectively) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 1.11 g (76 %) of *N*-[(*R*)-3-undecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 12 H), 1.0 - 1.65 (m, 88 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.1 - 2.5 (m,

8 H), 3.37 (m, 1 H), 3.64 (m, 1 H), 3.85 (m, 1 H), 4.30 (m, 3 H), 4.78 (m, 5 H), 5.18 (m, 4 H), 5.46 (m, 1 H), 6.07 (m, 1 H), 6.62 (d, 1 H, J = 7.7 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (1.0 g, 0.57 mmol) was deprotected with zinc (2.0 g, 30.5 mmol) and acylated with (*R*)-3-undecanoyloxytetradecanoic acid (280 mg, 0.68 mmol) in the presence of EEDQ (185 mg, 0.75 mmol) to afford 470 mg (50 %) of *N*-[(*R*)-3-undecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (470 mg, 0.27 mmol) was hydrogenated in the presence of palladium hydroxide on carbon in EtOH (10 mL) and platinum oxide (400 mg) in EtOH / AcOH (10:1) to afford 130 mg (30 %) of *N*-[(*R*)-3-undecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-undecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-undecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 181-183° C; IR (film) 3294, 2923, 2853, 1734, 1655, 1466, 1377, 1163, 1080, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.8 Hz), 1.1 - 1.7 (m, 117 H), 2.2 - 2.7 (m, 12 H), 3.06 (q, 6 H, J = 7.1 Hz), 3.4 - 3.2 (m, 5 H), 3.6 - 3.9 (m, 4 H), 4.20 (d, 1 H, 9.8 Hz), 4.54 (d, 1 H, J = 8.0 Hz), 4.62 (br. s, 1 H), 5.17 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.5, 173.3, 172.8, 172.2, 169.6, 169.1, 101.5, 77.2, 74.8, 70.9, 69.2, 60.5, 58.5, 53.1, 51.5, 46.1, 41.5, 41.1, 39.2, 34.6, 34.4, 34.1, 32.0, 29.8, 29.7, 29.4, 29.2, 25.6, 25.2, 25.1, 22.7, 18.5, 14.2, 8.7.

Anal. Calcd. for $C_{90}H_{172}N_3O_{19}P$: C, 66.26; H, 10.63; N, 2.58; P, 1.90. Found: C, 66.56; H, 10.57; N, 2.47; P, 1.91.

EXAMPLE 15 (B14)

Preparation of *N*-[(*R*)-3-Decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-D-serine Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), D-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (875 mg, 2.2 mmol) in the presence of EDC·MeI (745 mg, 2.5 mmol) in CH_2Cl_2 to afford 1.05 g (91 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-D-serine benzyl ester: mp 51-52 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 6 H), 1.1 - 1.7 (m, 34 H), 2.30 (t, 2 H, *J* = 7.7 Hz), 2.50 (m, 2 H),3.68 (s, 1 H), 3.93 (d, 2 H, *J* = 3.1 Hz), 4.62 (m, 1 H), 5.22 (m, 3 H), 6.63 (d, 1 H, *J* = 6.9 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (884 mg, 2.22 mmol) in the presence of EDC·MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in aqueous AcOH (25 mL) to afford 1.30g (77 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8 H), 1.25 (m, 30 H), 1.59 (m, 4 H), 2.30 (t, 2 H, *J* = 7.5 Hz), 2.52 (m, 2 H), 3.42 (m, 1 H), 3.55 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, *J* = 11.8, 4.6 Hz), 3.94 (m, 2 H), 4.57 (d, 1 H, *J* = 8.2 Hz), 4.71 (m, 2 H), 5.07 (m, 2 H), 5.27 (d, 1 H, *J* = 8.8 Hz).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.25g, 1.50 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (396 mg, 1.65 mmol) and pyridine (0.15 mL, 1.81 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.42 mL, 3.00 mmol), diphenyl chlorophosphate (0.47 mL, 2.25 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.31 g (69 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.89 (m, 8 H), 1.1 - 1.7 (m, 34 H), 1.82 (s, 3 H), 1.90 (s, 3 H),

2.30 (m, 4 H), 3.40 (q, 1 H, J = 9.6 Hz), 3.65 (m, 1 H), 3.89 (m, 1 H), 4.32 (m, 2 H), 4.63 (m, 2 H), 4.82 (d, 1 H, J = 12.1 Hz), 5.01 (d, 1 H, J = 8.2 Hz), 5.63 (m, 2 H), 7.29 (m, 10 H).

(4) In the same manner as described in Example 13-(4), the compound prepared in (3) above (1.27 g, 1.0 mmol) was deprotected with TFA (5 mL) and then treated with the Vilsmeier reagent generated from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) to give 1.06 g (89 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.6 Hz), 1.1 - 1.55 (m, 34 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, J = 7.7 Hz), 2.43 (m, 2 H), 4.32 (m, 4 H), 4.71 (m, 3 H), 4.83 (m, 3 H), 5.09 (m, 1 H), 5.50 (t, 1 H, J = 9.5 Hz), 5.77 (d, 1 H, J = 8.0 Hz), 6.26 (d, 1 H, J = 3.4 Hz), 7.20 (m, 10 H).

(5) In the same manner as described in Example 13-(5), compounds prepared in (1) and (4) above above (520 mg, 0.90 mmol, and 1.0 g, 0.84 mmol, respectively) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 1.13 g (78 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-D-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, J = 6.6 Hz), 1.1 - 1.65 (m, 68 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.2 - 2.6 (m, 8 H), 3.40 (m, 1 H), 3.64 (m, 1 H), 4.01 (m, 2 H), 4.27 (m, 2 H), 4.44 (d, 1 H, J = 7.1 Hz), 4.60 (m, 2 H), 4.77 (m, 2 H), 5.19 (m, 6 H), 6.61 (d, 1 H, J = 8.3 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (1.0 g, 0.58 mmol) was deprotected with zinc (1.9 g, 29 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (280 mg, 0.70 mmol) in the presence of EEDQ (190 mg, 0.77 mmol) to afford 420 mg (44 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-D-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (420 mg, 0.25 mmol) was hydrogenated in the presence of palladium hydroxide on carbon in EtOH (10 mL) and platinum oxide (400 mg) in EtOH / AcOH (10:1) to afford 118 mg (30 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-D-serine triethylammonium salt as a white powder: mp 179-181° C; IR (film) 3283, 3100, 2921, 2852, 1732, 1660, 1651, 1564, 1556, 1464, 1417, 1378, 1322, 1181, 1061, 856, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.8 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 12 H), 3.06 (m, 6 H), 3.33 (m, 5 H), 3.78 (m, 2 H), 3.95 (m, 2 H), 4.22 (m, 1 H), 4.45 (d, 1 H, *J* = 7.5 Hz), 4.68 (br. s, 1 H), 5.13 (m, 3 H), 5.26 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ δ 173.7, 173.5, 173.1, 171.1, 169.9, 100.3, 75.1, 73.9, 71.9, 71.1, 70.9, 70.2, 60.9, 53.9, 52.7, 46.0, 41.3, 40.8, 39.4, 34.6, 34.4, 31.9, 29.8, 29.7, 29.5, 29.4, 25.6, 25.4, 25.2, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{87}H_{166}N_3O_{19}P$: C, 65.75; H, 10.53; N, 2.64; P, 1.95. Found: C, 65.32; H, 10.28; N, 2.53; P, 1.89.

EXAMPLE 16 (B15)

Preparation of of *N*-[(*R*)-3-Decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt. (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (250 mg, 1.08 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (478 mg, 1.2 mmol) in the presence of EDC·MeI (357 mg, 1.2 mmol) in CH_2Cl_2 to afford 0.52 g (84 %) of *N*-[(*R*)-3-heptanoyloxytetradecanoyl]-L-serine benzyl ester: mp 52-53 °C; ^1H NMR ($CDCl_3$) δ 0.87 (t, 6 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 34 H), 2.29 (t, 2 H, *J* = 7.5 Hz), 2.49 (d, 2 H, *J* = 5.8 Hz), 3.67 (s, 1 H), 3.97 (m, 2 H), 4.63 (m, 1 H), 5.19 (m, 3 H), 6.61 (d, 1 H, *J* = 7.1 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (500 mg, 0.87 mmol), and the compound prepared in Example 15-(4) (1.08 g, 0.90 mmol) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 1.35 g (89 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-

diphenylphosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.6 Hz), 1.0 - 1.65 (m, 68 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.1 - 2.5 (m, 8 H), 3.38 (q, 1 H, *J* = 9.1 Hz), 3.65 (m, 1 H), 3.84 (m, 1 H), 4.27 (m, 3 H), 4.70 (m, 5 H), 4.84 (m, 4 H), 5.14 (m, 3 H), 5.46 (t, 1 H, *J* = 9.7 Hz), 6.07 (m, 1 H), 6.62 (d, 1 H, *J* = 8.0 Hz), 7.05 - 7.45 (m, 15 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (600 mg, 0.34 mmol) was deprotected with zinc (1.13 g, 17.2 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (150 mg, 0.38 mmol) in the presence of EEDQ (124 mg, 0.50 mmol) to afford 362 mg (60 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (300 mg, 0.17 mmol) was hydrogenated in the presence of palladium on carbon (100 mg) and platinum oxide (200 mg) in THF/AcOH (10:1) to afford 120 mg (44 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 175-176° C; IR (film) 3304, 2956, 2923, 2853, 1733, 1654, 1541, 1466, 1377, 1164, 1107, 1080, 845, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.75 (m, 12 H), 3.07 (q, 6 H, *J* = 7.2 Hz), 3.37 (m, 1 H), 3.5 - 3.95 (m, 8 H), 4.21 (q, 1 H, 11.0 Hz), 4.54 (d, 1 H, *J* = 8.9 Hz), 4.61 (br. s, 1 H), 5.17 (m, 4 H), 7.10 (d, 1 H, *J* = 9.0 Hz), 7.43 (d, 1 H, *J* = 7.9 Hz); ^{13}C NMR ($CDCl_3$) δ 176.3, 173.4, 173.2, 172.8, 172.0, 169.6, 169.2, 101.4, 74.7, 70.9, 69.3, 60.4, 53.2, 51.6, 46.1, 41.4, 41.0, 39.1, 34.5, 34.3, 34.2, 34.1, 31.9, 29.8, 29.7, 29.6, 29.4, 29.3, 29.2, 25.5, 25.1, 25.0, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{87}H_{166}N_3O_{19}P \cdot H_2O$: C, 65.01; H, 10.54; N, 2.61; P, 1.93. Found: C, 64.92; H, 10.38; N, 2.58; P, 2.06.

EXAMPLE 17 (B16)

Preparation of *N*-[(*R*)-3-Nonanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt. (Compound (I), R_1=R_2=R_3=*n*-$C_8H_{17}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-nonanoyloxytetradecanoic acid (780 mg, 2.2 mmol) in the presence of EDC·MeI (845 mg, 2.5 mmol) in CH_2Cl_2 to afford 1.0 g (89 %) of *N*-[(*R*)-3-nonanoyloxytetradecanoyl]-L-serine benzyl ester: mp 52-53 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.6 Hz), 1.1 - 1.7 (m, 32 H), 2.30 (t, 2 H, *J* = 7.7 Hz), 2.51 (d, 2 H, *J* = 5.8 Hz), 2.62 (t, 1 H, *J* = 6.0 Hz), 3.98 (m, 2 H), 4.65 (m, 1 H), 5.19 (m, 3 H), 6.58 (d, 1 H, *J* = 6.8 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-nonanoyloxytetradecanoic acid (852 mg, 2.22 mmol) in the presence of EDC·MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in aqueous AcOH (25 mL) to afford 1.31 g (79 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8 H), 1.25 (m, 28 H), 1.59 (m, 4 H), 2.30 (t, 2 H, *J* = 7.5 Hz), 2.52 (m, 2 H), 3.42 (m, 1 H), 3.55 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, *J* = 11.8, 4.6 Hz), 3.94 (m, 2 H), 4.57 (d, 1 H, *J* = 8.2 Hz), 4.71 (m, 2 H), 5.07 (m, 2 H), 5.27 (d, 1 H, *J* = 8.8 Hz).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.25 g, 1.52 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (400 mg, 1.67 mmol) and pyridine (0.15 mL, 1.84 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.42 mL, 3.04 mmol), diphenyl chlorophosphate (0.47 mL, 2.28 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.30 g (67 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 8 H), 1.1 - 1.7 (m, 32 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.22 (m, 6 H), 3.33 (m, 1 H), 3.53 (m, 1 H), 3.80 (m, 1 H), 3.96 (m, 1 H), 4.31 (m, 2 H),

4.55 (m, 2 H), 4.83 (d, 1 H, J = 12.0 Hz), 5.01 (d, 1 H, J = 7.9 Hz), 5.62 (m, 1 H), 7.28 (m, 10 H).

(4) In the same manner as described in Example 13-(4), the compound prepared in (3) above (1.26 g, 1.0 mmol) was deprotected with TFA (5 mL) and then treated with the Vilsmeier reagent generated from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) to give 1.07 g (91 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.9 Hz), 1.25 - 1.55 (m, 32 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, J = 7.7 Hz), 2.43 (m, 2 H), 4.34 (m, 4 H), 4.70 (m, 3 H), 4.83 (m, 3 H), 5.09 (m, 1 H), 5.51 (t, 1 H, J = 10.2 Hz), 5.78 (d, 1 H, J = 8.0 Hz), 6.25 (d, 1 H, J = 3.6 Hz), 7.19 (m, 10 H).

(5) In the same manner as described in Example 13-(5), compounds prepared in (1) and (4) above (505 mg, 0.90 mmol, and 1.0 g, 0.85 mmol, respectively) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 1.03 g (71 %) of *N*-[(*R*)-3-nonanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, J = 6.9 Hz), 1.0 - 1.65 (m, 64 H), 1.78 (s, 3 H), 1.82 (s, 3 H), 2.1 - 2.5 (m, 8 H), 3.38 (m, 1 H), 3.64 (m, 1 H), 3.83 (m, 1 H), 4.25 (m, 3 H), 4.73 (m, 5 H), 5.18 (m, 5 H), 6.07 (m, 1 H), 6.60 (d, 1 H, J = 7.8 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (1.0 g, 0.59 mmol) was deprotected with zinc (1.93 g, 29.5 mmol) and acylated with (*R*)-3-nonanoyloxytetradecanoic acid (273 mg, 0.71 mmol) in the presence of EEDQ (195 mg, 0.78 mmol) to afford 405 mg (42 %) of *N*-[(*R*)-3-nonanoyloxytetradecanoyl]-*O*-[deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (405 mg, 0.25 mmol) was hydrogenated in the presence of palladium hydroxide on carbon in EtOH (10 mL) and platinum oxide (400 mg) in EtOH

/ AcOH (10:1) to afford 185 mg (48 %) of *N*-[(*R*)-3-nonanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-nonanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-nonanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 177-179° C; IR (film) 3306, 2955, 2923, 2853, 1732, 1660, 1538, 1467, 1378, 1252, 1165, 1106, 1080, 960, 844, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.8 Hz), 1.1 - 1.7 (m, 105 H), 2.2 - 2.75 (m, 12 H), 3.07 (q, 6 H, *J* = 7.1 Hz), 3.2 - 3.5 (m, 5 H), 3.85 (m, 4 H), 4.23 (d, 1 H, 10.2 Hz), 4.51 (d, 1 H, *J* = 8.0 Hz), 4.64 (br. s, 1 H), 5.18 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.3, 172.8, 172.2, 169.6, 169.1, 101.5, 74.8, 70.9, 70.8, 69.3, 60.5, 53.2, 51.5, 46.1, 41.5, 41.0, 39.2, 34.5, 34.3, 34.1, 32.0, 31.9, 29.8, 29.6, 29.4, 29.3, 25.6, 25.2, 25.1, 22.7, 14.1, 8.7.

Anal. Calcd. for $C_{84}H_{160}N_3O_{19}P$: C, 65.21; H, 10.42; N, 2.72; P, 2.00. Found: C, 65.48; H, 10.32; N, 2.62; P, 2.12.

EXAMPLE 18 (B17)

Preparation of *N*-[(*R*)-3-Octanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-octanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_7H_{15}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-octanoyloxytetradecanoic acid (815 mg, 2.2 mmol) in the presence of EDC·MeI (745 mg, 2.5 mmol) in CH_2Cl_2 to afford 1.02 g (93 %) of *N*-[(*R*)-3-octanoyloxytetradecanoyl]-L-serine benzyl ester: mp 50-51 °C; ^1H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.8 Hz), 1.1 - 1.7 (m, 30 H), 2.30 (t, 2 H, *J* = 7.7 Hz), 2.51 (d, 2 H, *J* = 5.8 Hz), 2.60 (t, 1 H, *J* = 6.0 Hz), 3.97 (m, 2 H), 4.65 (m, 1 H), 5.22 (m, 3 H), 6.61 (d, 1 H, *J* = 6.9 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-octanoyloxytetradecanoic acid (821 mg, 2.22 mmol) in the presence of EDC·MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in 90 % aqueous AcOH (25 mL) to afford 1.35g (83 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8

H), 1.25 (m, 26 H), 1.60 (m, 4 H), 2.30 (t, 2 H, J = 7.5 Hz), 2.53 (m, 2 H), 3.42 (m, 1 H), 3.53 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, J = 11.8, 4.4 Hz), 3.94 (m, 2 H), 4.56 (d, 1 H, J = 8.3 Hz), 4.64 (d, 1 H, J = 11.8 Hz), 4.77 (d, 1 H, J = 11.8 Hz), 5.08 (m, 2 H), 5.30 (br. s, 1 H).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.30 g, 1.61 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (425 mg, 1.77 mmol) and pyridine (0.16 mL, 1.95 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.45 mL, 3.22 mmol), diphenyl chlorophosphate (0.50 mL, 2.42 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.42 g (71 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 8 H), 1.1 - 1.7 (m, 30 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.23 (m, 6 H), 3.37 (m, 1 H), 3.65 (m, 1 H), 3.83 (m, 1 H), 3.96 (m, 1 H), 4.55 (m, 2 H), 4.83 (d, 1 H, J = 11.8 Hz), 5.01 (d, 1 H, J = 8.2 Hz), 5.20 (m, 1 H), 7.29 (m, 10 H).

(4) In the same manner as described in Example 13-(4), the compound prepared in (3) above (1.24 g, 1.0 mmol) was deprotected with TFA (5 mL) and then treated with the Vilsmeier reagent generated from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) to give 1.0 g (87 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.7 Hz), 1.25 - 1.55 (m, 30 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, J = 7.7 Hz), 2.43 (m, 2 H), 4.29 (m, 4 H), 4.72 (m, 3 H), 5.09 (m, 1 H), 5.51 (t, 1 H, J = 9.9 Hz), 5.79 (d, 1 H, J = 7.9 Hz), 6.25 (d, 1 H, J = 3.5 Hz), 7.29 (m, 10 H).

(5) In the same manner as described in Example 13-(5), compounds prepared in (1) and (4) above (490 mg, 0.90 mmol, and 1.0 g, 0.86 mmol, respectively) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 0.99 g (69 %) of *N*-[(*R*)-3-octanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR

($CDCl_3$) δ 0.88 (t, 12 H, J = 6.9 Hz), 1.0 - 1.65 (m, 60 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.1 - 2.5 (m, 8 H), 3.37 (m, 1 H), 3.65 (m, 1 H), 3.83 (m, 1 H), 4.27 (m, 3 H), 4.72 (m, 5 H), 5.18 (m, 4 H), 5.46 (t, 1 H, J = 9.8 Hz), 6.06 (m, 1 H), 6.60 (d, 1 H, J = 8.0 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (0.95 g, 0.57 mmol) was deprotected with zinc (1.86 g, 28.5 mmol) and acylated with (*R*)-3-octanoyloxytetradecanoic acid (252 mg, 0.68 mmol) in the presence of EEDQ (185 mg, 0.75 mmol) to afford 433 mg (47 %) of *N*-[(*R*)-3-octanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-octanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (433 mg, 0.27 mmol) was hydrogenated in the presence of palladium hydroxide on carbon (250 mg) in EtOH (10 mL) and platinum oxide (400 mg) in EtOH / AcOH (10:1) to afford 196 mg (48 %) of *N*-[(*R*)-3-octanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-octanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-octanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 177-178° C; IR (film) 3296, 2956, 2923, 2853, 1732, 1645, 1546, 1466, 1378, 1315, 1170, 1082, 1056, 961, 846, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.6 Hz), 1.1 - 1.7 (m, 99 H), 2.2 - 2.75 (m, 12 H), 3.08 (q, 6 H, J = 7.1 Hz), 3.39 (d, 1 H, J = 8.8 Hz), 3.6 - 4.0 (m, 8 H), 4.22 (q, 1 H, 10.3 Hz), 4.53 (d, 1 H, J = 8.2 Hz), 4.63 (m, 1 H), 5.18 (m, 4 H), 7.04 (d, 1 H, J = 8.8 Hz), 7.42 (d, 1 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 176.8, 173.3, 173.2, 172.7, 172.2, 169.6, 169.1, 101.5, 74.8, 70.9, 70.8, 69.3, 60.5, 53.2, 51.5, 46.2, 41.5, 41.1, 39.2, 34.5, 34.3, 34.1, 34.0, 32.0, 31.8, 29.8, 29.6, 29.4, 29.3, 29.2, 29.1, 25.6, 25.3, 25.2, 25.0, 22.7, 14.1, 8.7.

Anal. Calcd. for $C_{81}H_{154}N_3O_{19}P \cdot H_2O$: C, 63.87; H, 10.32; N, 2.76; P, 2.03. Found: C, 63.96; H, 10.29; N, 2.69; P, 1.67.

EXAMPLE 19 (B18)

Preparation of *N*-[(*R*)-3-Heptanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_6H_{13}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2H, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), L-serine benzyl ester (390 mg, 2.0 mmol) was acylated with (*R*)-3-heptanoyloxytetradecanoic acid (780 mg, 2.2 mmol) in the presence of EDC·MeI (745 mg, 2.5 mmol) in CH_2Cl_2 to afford 0.97 g (91 %) of *N*-[(*R*)-3-heptanoyloxytetradecanoyl]-L-serine benzyl ester: mp 46-48 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 28 H), 2.30 (t, 2 H, *J* = 7.7 Hz), 2.50 (d, 2 H, *J* = 5.8 Hz), 2.62 (t, 1 H, *J* = 6.0 Hz), 3.97 (m, 2 H), 4.65 (m, 1 H), 5.19 (m, 3 H), 6.61 (d, 1 H, *J* = 6.9 Hz), 7.35 (br s, 5 H).

(2) In the same manner as described in Example 2-(2), the compound prepared in Example 2-(1) (1.0 g, 2.02 mmol) was acylated with (*R*)-3-heptanoyloxytetradecanoic acid (790 mg, 2.22 mmol) in the presence of EDC·MeI (720 mg, 2.4 mmol) and 4-pyrrolidinopyridine (100 mg) in CH_2Cl_2, and then deprotected in 90 % aqueous AcOH (25 mL) to afford 1.30g (81 %) of 2-(trimethylsilyl)ethyl 2-deoxy-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9 H), 0.88 (m, 8 H), 1.25 (m, 24 H), 1.59 (m, 4 H), 2.30 (t, 2 H, *J* = 7.5 Hz), 2.52 (m, 2 H), 3.42 (m, 1 H), 3.55 (m, 1 H), 3.66 (m, 1 H), 3.83 (dd, 1 H, *J* = 11.5, 4.2 Hz), 3.94 (m, 2 H), 4.57 (d, 1 H, *J* = 8.3 Hz), 4.64 (d, 1 H, *J* = 12.1 Hz), 4.76 (d, 1 H, *J* = 11.9 Hz), 5.09 (m, 2 H), 5.31 (d, 1 H, *J* = 8.7 Hz).

(3) In the same manner as described in Example 2-(3), the compound prepared in (2) above (1.25g, 1.58 mmol) was treated with 2,2,2-trichloro-1,1-dimethylethyl chloroformate (417 mg, 1.74 mmol) and pyridine (0.15 mL, 1.91 mmol) in CH_2Cl_2 (25 mL) followed by triethylamine (0.44 mL, 3.16 mmol), diphenyl chlorophosphate (0.49 mL, 2.37 mmol) and 4-pyrrolidinopyridine (100 mg) to afford 1.34 g (69 %) of 2-(trimethylsilyl)ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9 H), 0.88 (m, 8 H), 1.1 - 1.7 (m, 28 H), 1.82 (s, 3 H), 1.89 (s, 3 H),

2.35 (m, 4 H), 3.37 (m, 1 H), 3.61 (m, 1 H), 3.80 (m, 1 H), 4.32 (m, 2 H), 4.63 (m, 2 H), 4.83 (d, 1 H, J = 12.0 Hz), 5.01 (d, 1 H, J = 8.2 Hz), 5.62 (m, 2 H), 7.29 (m, 10 H).

(4) In the same manner as described in Example 13-(4), the compound prepared in (3) above (1.23 g, 1.0 mmol) was deprotected with TFA (5 mL) and then treated with the Vilsmeier reagent generated from DMF (0.39 mL, 5.0 mmol) and oxalyl chloride (0.22 mL, 2.5 mmol) to give 1.0 g (87 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J = 6.9 Hz), 1.25 - 1.55 (m, 28 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, J = 7.6 Hz), 2.43 (m, 2 H), 4.26 (m, 4 H), 4.73 (m, 3 H), 5.09 (m, 1 H), 5.51 (t, 1 H, J = 10.2 Hz), 5.77 (d, 1 H, J = 8.0 Hz), 6.25 (d, 1 H, J = 3.3 Hz), 7.19 (m, 10 H).

(5) In the same manner as described in Example 13-(5), compounds prepared in (1) and (4) above (480 mg, 0.90 mmol, and 0.98g, 0.86 mmol, respectively) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to afford 1.06 g (75 %) of *N*-[(*R*)-3-heptanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenyl phosphono-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine benzyl ester: ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 12 H), 1.0 - 1.65 (m, 56 H), 1.77 (s, 3 H), 1.85 (s, 3 H), 2.1 - 2.5 (m, 8 H), 3.38 (m, 1 H), 3.64 (m, 1 H), 3.83 (m, 1 H), 4.25 (m, 3 H), 4.78 (m, 5 H), 5.16 (m, 4 H), 5.46 (t, 1 H, J = 9.9 Hz), 6.06 (m, 1 H), 6.60 (d, 1 H, J = 7.7 Hz), 7.05 - 7.45 (m, 15 H).

(6) In the same manner as described in Example 2-(7), the compound prepared in (5) above (1.0 g, 0.61 mmol) was deprotected with zinc (2.0 g, 30.5 mmol) and acylated with (*R*)-3-heptanoyloxytetradecanoic acid (260 mg, 0.73 mmol) in the presence of EEDQ (200 mg, 0.80 mmol) to afford 440 mg (45 %) of *N*-[(*R*)-3-heptanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine benzyl ester as an amorphous solid.

(7) In the same manner as described in Example 2-(8), the compound prepared in (6) above (440 mg, 0.28 mmol) was hydrogenated in the presence of

palladium hydroxide on carbon (250 mg) in EtOH (10 mL) and platinum oxide (400 mg) in EtOH / AcOH (10:1) to afford 208 mg (51 %) of *N*-[(*R*)-3-heptanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-heptanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-heptanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine triethylammonium salt as a white powder: mp 176-177° C; IR (film) 3307, 2956, 2924, 2854, 1732, 1650, 1545, 1466, 1378, 1316, 1170, 1080, 956, 841, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (m, 18 H), 1.1 - 1.7 (m, 93 H), 2.2 - 2.75 (m, 12 H), 3.08 (q, 6 H, *J* = 7.2 Hz), 3.40 (d, 1 H, *J* = 10.2 Hz), 3.6 - 4.0 (m, 7 H), 4.24 (m, 2 H), 4.52 (d, 1 H, *J* = 8.0 Hz), 4.63 (m, 1 H), 5.19 (m, 4 H), 7.04 (d, 1 H, *J* = 8.6 Hz), 7.40 (d, 1 H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 177.1, 173.2, 173.1, 172.7, 172.3, 169.5, 168.9, 101.5, 75.0 74.8, 71.2, 70.9, 69.1, 60.5, 53.1, 51.4, 46.1, 41.5, 41.0, 39.2, 34.5, 34.3, 34.1, 34.0, 31.9, 31.6, 31.5, 29.8, 29.6, 29.4, 29.0, 28.9, 28.8, 25.6, 25.3, 25.1, 25.0, 22.7, 22.6, 14.1, 8.7.

Anal. Calcd. for $C_{78}H_{148}N_3O_{15}P$: C, 64.04; H, 10.20; N, 2.87; P, 2.12. Found: C, 63.77; H, 10.11; N, 2.85; P, 2.02.

EXAMPLE 20 (B19)

Preparation of 2-[(*R*)-3-Tetradecanoyloxytetradecanoylamino]ethyl 2-Deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyoxytetradecanoylamino]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_6=R_7=R_9=H, R_8=PO_3H_2).

(1) 2-Amino-1-(*t*-butyldiphenylsilyloxy)ethane (330 mg, 1.1 mmol) and (*R*)-3-tetradecanoyloxytetradecanoic acid (500 mg, 1.1 mmol) were dissolved in CH_2Cl_2 (10 mL) and treated with powdered 4 A molecular sieves (500 mg). After 1 h EEDQ (297 mg, 1.2 mmol) was added and the reaction was stirred for 18 h, filtered through Celite® and concentrated *in vacuo*. The residue was chromatographed over silica gel using 15 % EtOAc / hexanes to give 675 mg (92 %) of a colorless solid. A portion of this material (500 mg, 0.68 mmol) was deprotected with TBAF (1 M in THF, 1 mL, 1 mmol) in THF (5 mL) by stirring at room temperature for 2 h. The reaction mixture was diluted with Et_2O (50 mL) and washed with brine (2 x 50 mL). The brine was back extracted with Et_2O (2 x 50 mL) and the combined organic extracts were dried over Na_2SO_4 and

concentrated *in vacuo* to afford 338 mg (62 %) of 2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]ethanol as an off-white solid.

(2) In the same manner as described in Example 2-(6), the compound prepared in (1) above (338 mg, 0.68 mmol) and the compound prepared in Example 2-(4) (786 mg, 0.61 mmol) were coupled in the presence of mercury cyanide (770 mg, 3.05 mmol) to give 245 mg (24%) of 2-[*(R)*-3-tetradecanoyloxytetradecanoylamino]ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[*(R)*-3-tetradecanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.9 Hz), 1.1 - 1.8 (m, 84 H), 1.81 (s, 3 H), 1.89 (s, 3 H), 2.15 - 2.55 (m, 8 H), 3.25 (m, 1 H), 3.47 (m, 2 H), 3.67 (m, 1 H), 3.83 (m, 2 H), 4.28 (dd, 1 H, *J* = 12.2, 4.9 Hz), 4.36 (d, 1 H, *J* = 11.0 Hz), 4.68 (m, 2 H), 4.78 (d, 1 H, *J* = 11.6 Hz), 4.94 (d, 1 H, *J* = 11.6 Hz), 5.16 (m, 2 H), 5.53 (t, 1 H, *J* = 10.0 Hz), 6.06 (d, 1 H, *J* = 4.9 Hz), 6.19 (m, 1 H), 7.25 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (500 mg, 0.29 mmol) was deprotected with zinc (980 mg, 15 mmol) and then acylated with *(R)*-3-tetradecanoyloxytetradecanoic acid (155 mg, 0.34 mmol) in the presence of EEDQ (110 mg, 0.44 mmol) to give 315 mg (62%) of 2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]ethyl2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyoxytetradecanoylamino]-β-D-glucopyranoside as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (200 mg, 0.113 mmol) was hydrogenated in the presence of platinum oxide (100 mg) to give 142 mg (76 %) of 2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]ethyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyoxytetradecanoylamino]-β-D-glucopyranoside triethylammonium salt as a white solid: mp 175-176° C; IR (film) 3285, 3098, 2955, 2919, 2851, 1731, 1659, 1642, 1556, 1468, 1379, 1250, 1228, 1174, 1110, 1083, 1046, 962, 857 cm^{-1}; ^{1}H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.0 Hz), 1.1 - 1.7 (m, 135 H), 2.2 - 2.7 (m, 15 H), 3.06 (q, 6 H, *J* = 7.1 Hz), 3.2 - 4.1 (m, 8 H), 4.21 (q, 1 H, *J* = 9.9 Hz), 4.51 (d, 1 H, *J* = 8.2 Hz), 5.05 - 5.25 (m, 4 H), 7.33 (d, 1 H, *J* = 8.5 Hz), 7.50 (br t, 1 H, *J* = 4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 173.7, 173.3, 170.6, 170.3, 169.9, 100.9,

75.8, 73.0, 71.3, 71.1, 70.9, 70.6, 68.3, 60.6, 55.1, 45.7, 41.6, 41.2, 39.5, 34.6, 34.5, 34.4, 32.0, 29.8, 29.4, 29.3, 25.4, 25.1, 22.7, 14.2, 8.6.

Anal. Calcd. for $C_{98}H_{190}N_3O_{17}P \cdot 2\ H_2O$: C, 67.28; H, 11.18; N, 2.40; P, 1.77. Found: C, 67.01; H, 11.18; N, 2.15; P, 2.01.

EXAMPLE 21 (B20)

Preparation of 2-[(*R*)-3-Decanoyloxytetradccanoylamino]ethyl 2-Deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-2-[(*R*)-3-decanoyloxytetradecanoylamino]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_6=R_7=R_9=H, R_8=PO_3H_2).

(1) In the same manner as described in Example 20-(1), 2-amino-1-(*t*-butyldiphenylsilyloxy)ethane (450 mg, 1.5 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (600 mg, 1.5 mmol) in the presence of EDC·MeI (594 mg, 2.0 mmol) and then deprotected with TBAF (1.0 M in THF, 2.5 mL, 2.5 mmol) in THF (10 mL) to afford 488 mg (81 %) of 2-[(*R*)-3-decanoyloxytetradecanoylamino]ethanol as an off-white solid.

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (385 g, 0.87 mmol) and the compound prepared in Example 15-(4) (1.05 g, 0.87 mmol) were coupled in the presence of AgOTf (560 mg, 2.2 mmol) to give 1.04 g (74 %) of 2-[(*R*)-3-decanoyloxytetradecanoylamino]ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.9 Hz), 1.1 - 1.6 (m, 68 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, *J* = 7.7 Hz), 2.44 (m, 2 H), 4.34 (m, 5 H), 4.72 (m, 2 H), 4.83 (q, 1 H, *J* = 9.3 Hz), 5.09 (m, 1 H), 5.51 (t, 1 H, *J* = 10.2 Hz), 5.79 (d, 1 H, *J* = 8.0 Hz), 6.26 (d, 1 H, *J* = 3.4 Hz), 7.31 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (700 mg, 0.44 mmol) was deprotected with zinc (1.42 g, 21.7 mmol) and then acylated with (*R*)-3-decanoyloxytetradecanoic acid (190 mg, 0.48 mmol) in the presence of EEDQ (148 mg, 0.6 mmol) to give 432 mg (62 %) of 2-[(*R*)-3-decanoyloxytetradecanoylamino]ethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-

decanoyoxytetradecanoyl]-2-[(*R*)-3-decanoyloxytetradecanoylamino]-β-D-glucopyranoside as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (400 mg, 0.25 mmol) was hydrogenated in the presence of platinum oxide (200 mg) to give 200 mg (52 %) of 2-[(*R*)-3-decanoyloxytetradecanoylamino]ethyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-2-[(*R*)-3-decanoyloxytetradecanoylamino]-β-D-glucopyranoside triethylammonium salt as a white solid: mp 165-166° C; IR (film) 3289, 3094, 2956, 2922, 2853, 1732, 1658, 1644, 1556, 1467, 1379, 1247, 1164, 1107, 1081, 1048 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 15 H), 3.05 (q, 6 H, *J* = 7.1 Hz), 3.2 - 3.85 (m, 9 H), 4.52 (d, 1 H, *J* = 8.2 Hz), 5.05 - 5.25 (m, 4 H), 7.21 (d, 1 H, *J* = 8.5 Hz), 7.42 (br t, 1 H); ^{13}C NMR ($CDCl_3$) δ 173.8, 173.3, 170.7, 170.3, 170.0, 100.9, 75.6, 73.0, 71.3, 70.9, 70.6, 68.3, 60.7, 55.0, 45.8, 41.6, 41.2, 39.5, 34.5, 34.4, 34.1, 31.9, 29.8, 29.6, 29.5, 29.4, 25.4, 25.1, 22.7, 14.2, 8.6.

Anal. Calcd. for $C_{86}H_{166}N_3O_{17}P \cdot H_2O$: C, 66.08; H, 10.83; N, 2.69; P, 1.98. Found: C, 65.80; H, 10.63; N, 2.63; P, 2.04.

EXAMPLE 22 (B21)

Preparation of 3-[(*R*)-3-Tetradecanoyloxytetradecanoylamino]propyl 2-Deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=1, m=p=q=0, R_4=R_5=R_6=R_7=R_9=H, R_8=PO_3H_2).

(1) In the same manner as described in Example 20-(1), 3-amino-1-(*t*-butyldiphenylsilyloxy)propane (470 mg, 1.5 mmol) was acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (680 mg, 1.5 mmol) in the presence of EDC·MeI (595 mg, 2.0 mmol) and then deprotected with TBAF (1.0 M in THF, 2.0 mL, 2.0 mmol) in THF (10 mL) to afford 698 mg (91 %) of 3-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-1-propanol as an off-white solid.

(2) In the same manner as described in Example 13-(4), the compound prepared in Example 2-(3) (7.9 g, 5.88 mmol) was deprotected with TFA (10 mL) and then treated with the Vilsmeier reagent generated from DMF (1.8 mL, 23.5 mmol) and

oxalyl chloride (1.03 mL, 11.76 mmol) in CH_2Cl_2 (60 mL) to give 6.32 g (85 %) of 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl chloride as a white foam: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, *J* = 6.8 Hz), 1.2 - 1.55 (m, 42 H), 1.78 (s, 3 H), 1.88 (s, 3 H), 2.18 (t, 2 H, *J* = 7.5 Hz), 2.43 (m, 2 H), 4.31 (m, 4 H), 4.68 (d, 1 H, *J* = 11.9 Hz), 4.74 (d, 1 H, *J* = 11.9 Hz), 4.83 (q, 1 H, *J* = 9.3 Hz), 5.09 (m, 1 H), 5.51 (t, 1 H, *J* = 9.7 Hz), 5.78 (d, 1 H, *J* = 8.0 Hz), 6.26 (d, 1 H, *J* = 3.4 Hz), 7.31 (m, 10 H).

(3) In the same manner as described in Example 13-(5), the compound prepared in (1) above (613 mg, 1.2 mmol) and the compound prepared in (2) above (1.5 g, 1.2 mmol) were coupled in the presence of AgOTf (642 mg, 2.5 mmol) to give 1.43 g (68 %) of 3-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.9 Hz), 1.1 - 1.8 (m, 86 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.20 (t, 2 H, *J* = 7.6 Hz), 2.29 (t, 2 H, *J* = 7.7 Hz), 2.44 (m, 4 H), 3.21 (m, 1 H), 3.42 (m, 1 H), 3.54 (m, 2 H), 3.80 (m, 1 H), 3.94 (m, 1 H), 4.28 (dd, 1 H, *J* = 12.3, 5.2 Hz), 4.38 (d, 1 H, *J* = 10.8 Hz), 4.70 (m, 3 H), 4.81 (d, 1 H, *J* = 8.2 Hz), 5.14 (m, 2 H), 5.47 (t, 1 H, *J* = 9.6 Hz), 6.13 (d, 1 H, *J* = 7.6 Hz), 6.22 (br. s, 1 H), 7.25 (m, 10 H).

(4) In the same manner as described in Example 2-(7), the compound prepared in (3) above (700 mg, 0.40 mmol) was deprotected with zinc (1.32 g, 20.1 mmol) and then acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (200 mg, 0.44 mmol) in the presence of EEDQ (125 mg, 0.5 mmol) to give 435 mg (60 %) of 3-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside as an amorphous solid.

(5) In the same manner as described in Example 2-(8), the compound prepared in (4) above (400 mg, 0.22 mmol) was hydrogenated in the presence of platinum oxide (200 mg) to give 170 mg (45 %) of 3-[(*R*)-3-tetradecanoyloxytetradecanoylamino]propyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-

tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside triethylammonium salt as a white solid: mp 171-172° C; IR (film) 3288, 3094, 2955, 2919, 2850, 1731, 1658, 1344, 1556, 1468, 1378, 1320, 1251, 1226, 1172, 1106, 1083, 1044 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.0 Hz), 1.1 - 1.7 (m, 135 H), 2.2 - 2.7 (m, 15 H), 3.06 (q, 6 H, J = 7.1 Hz), 3.2 - 4.1 (m, 8 H), 4.21 (q, 1 H, J = 9.9 Hz), 4.51 (d, 1 H, J = 8.3 Hz), 5.05 - 5.25 (m, 4 H), 7.23 (t, 1 H, J = 5.3 Hz), 7.33 (d, 1 H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 173.5, 173.4, 170.6, 170.2, 169.9, 100.6, 75.8, 71.5, 70.9, 70.5, 66.8, 60.4, 55.3, 45.6, 41.4, 39.4, 36.3, 34.6, 34.5, 34.2, 31.9, 29.7, 29.4, 29.3, 29.1, 25.4, 25.1, 22.7, 14.1, 8.5.

Anal. Calcd. for $C_{99}H_{192}N_3O_{17}P \cdot 2\ H_2O$: C, 67.42; H, 11.20; N, 2.38; P, 1.76. Found: C, 66.97; H, 11.01; N, 2.38; P, 1.95.

EXAMPLE 23 (B22)

Preparation of 4-[(*R*)-3-Tetradecanoyloxytetradecanoylamino]butyl 2-Deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_{13}H_{27}CO$, X=Y=O, n=2, m=p=q=0, R_4=R_5=R_6=R_7=R_9=H, R_8=PO_3H_2).

(1) In the same manner as described in Example 20-(1), 4-amino-1-(*t*-butyldiphenylsilyloxy)butane (500 mg, 1.53 mmol) was acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (695 mg, 1.53 mmol) in the presence of EDC·MeI (595 mg, 2.0 mmol) and then deprotected with TBAF (1.0 M in THF, 2.5 mL, 2.5 mmol) in THF (15 mL) to afford 651 mg (81 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-1-butanol as an off-white solid.

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (650 mg, 1.25 mmol) and the compound prepared in Example 22-(2) (1.6 g, 1.25 mmol) were coupled in the presence of AgOTf (1.16 g, 4.5 mmol) to give 1.65 g (75 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]butyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^1H NMR ($CDCl_3$) δ 0.88 (t, 12 H, J = 6.9 Hz), 1.1 - 1.8 (m, 88 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.15 - 2.55 (m, 8 H), 3.24 (m, 2 H), 3.50 (m, 2 H), 3.83

(m, 2 H), 4.27 (dd, 1 H, J = 12.1, 3.8 Hz), 4.32 (d, 1 H, J = 11.5 Hz), 4.66 (m, 2 H), 4.78 (d, 1 H, J = 12.1 Hz), 4.89 (d, 1 H, J = 8.0 Hz), 5.15 (m, 2 H), 5.54 (t, 1 H, J = 9.7 Hz), 5.95 (m, 2 H), 7.25 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (700 mg, 0.39 mmol) was deprotected with zinc (1.30 g, 19.8 mmol) and then acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (195 mg, 0.43 mmol) in the presence of EEDQ (125 mg, 0.5 mmol) to give 421 mg (60 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]butyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (400 mg, 0.22 mmol) was hydrogenated in the presence of platinum oxide (200 mg) to give 212 mg (55 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]butyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside triethylammonium salt as a white solid: mp 171-172° C; IR (film) 3298, 2955, 2920, 2851, 1732, 1645, 1550, 1467, 1378, 1181, 1107, 1083, 1044, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.9 Hz), 1.1 - 1.7 (m, 135 H), 2.2 - 2.7 (m, 19 H), 3.05 (q, 6 H, J = 7.1 Hz), 3.18 (m, 2 H), 3.3 - 3.5 (m, 6 H), 3.78 (m, 3 H), 3.97 (d, 1 H, J = 12.5 Hz), 4.23 (q, 1 H, J = 10.0 Hz), 4.50 (d, 1 H, J = 8.5 Hz), 5.13 (m, 4 H), 7.12 (d, 1 H, J = 9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 173.9, 173.4, 173.3, 170.8, 169.9, 169.8, 101.0, 75.6, 73.2, 71.4, 71.1, 70.6, 68.9, 60.7, 54.8, 45.9, 41.5, 39.6, 38.9, 34.6, 34.3, 32.0, 29.8, 29.5, 29.0, 28.9, 26.3, 25.4, 25.1, 22.7, 14.2, 8.7.

Anal. Calcd. for $C_{106}H_{194}N_3O_{17}P \cdot H_2O$: C, 68.26; H, 11.23; N, 2.39; P, 1.76. Found: C, 68.21; H, 11.03; N, 2.26; P, 1.73.

EXAMPLE 24 (B23)

Preparation of 4-[(*R*)-3-Tetradecanoyloxytetradecanoylamino]hexyl 2-Deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=4, m=p=q=0, R_4=R_5=R_6=R_7=R_9=H, R_8=PO_3H_2).

(1) In the same manner as described in Example 20-(1), 6-amino-1-(*t*-butyldiphenylsilyloxy)hexane (1.48 g, 4.15 mmol) was acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (2.07g, 4.56 mmol) in the presence of EDC·MeI (1.35g, 4.56 mmol) and then deprotected with TBAF (1.0 M in THF, 1.53 mL, 1.53 mmol) in THF (46 mL) to afford 700 mg (30 %) of 6-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-1-hexanol as an off-white solid.

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (689 mg, 1.20 mmol) and the compound prepared in Example 22-(2) (1.25 g, 1.00 mmol) were coupled in the presence of AgOTf (1.28 g, 5.0 mmol) to give 1.59 g (94 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]hexyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J* = 6.6 Hz), 1.1 - 1.8 (m, 92 H), 1.82 (s, 3 H), 1.89 (s, 3 H), 2.22 (t, 2 H, *J* = 7.6 Hz), 2.29 (t, 2 H, *J* = 7.4 Hz), 2.45 (m, 4 H), 3.22 (m, 1 H), 3.46 (m, 2 H), 3.83 (m, 2 H), 3.94 (m, 1 H), 4.31 (m, 2 H), 4.64 (m, 2 H), 4.83 (d, 1 H, *J* = 12.1 Hz), 4.97 (d, 1 H, *J* = 7.8 Hz), 5.17 (m, 2 H), 5.59 (t, 1 H, *J* = 8.8 Hz), 5.75 (m, 1 H), 5.84 (d, 1 H, *J* = 7.6 Hz), 7.25 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (1.57 g, 0.88 mmol) was deprotected with zinc (2.88 g, 44.1 mmol) and then acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (481 mg, 1.06 mmol) in the presence of EEDQ (327 mg, 1.32 mmol) to give 1.57 g (97 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]hexyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino])-β-D-glucopyranoside as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (1.57 g, 0.85 mmol) was hydrogenated in the presence of platinum

oxide (157 mg) to give 130 mg (10 %) of 4-[(*R*)-3-tetradecanoyloxytetradecanoylamino]hexyl 2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyoxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranoside triethylammonium salt as a white solid: mp 150-152° C; IR (film) 3284, 3099, 2954, 2920, 2851, 1731, 1657, 1637, 1557, 1467, 1418, 1378, 1320, 1249, 1179, 1108, 1083, 1044, 856, 721 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.89 (t, 18 H, *J* = 6.6 Hz), 1.1 - 1.7 (m, 135 H), 2.2 - 2.7 (m, 23 H), 3.05 (q, 6 H, *J* = 7.1 Hz), 3.18 (m, 2 H), 3.39 (d, 1 H, *J* = 8.2 Hz), 3.49 (q, 1 H, *J* = 7.5 Hz), 3.82 (m, 2 H), 3.99 (d, 1 H, *J* = 11.9 Hz), 4.25 (q, 1 H, *J* = 8.9 Hz), 4.59 (m, 2 H), 5.18 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.7, 173.3, 170.6, 169.7, 169.4, 100.6, 75.5, 73.1, 71.3, 70.9, 70.6, 69.2, 60.6, 55.2, 45.8, 41.7, 41.4, 39.5, 39.4, 34.6, 34.3, 34.2, 34.1, 31.9, 29.7, 29.4, 29.2, 26.5, 25.5, 25.3, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{102}H_{198}N_3O_{17}P \cdot H_2O$: C, 68.53; H, 11.28; N, 2.33; P, 1.73. Found: C, 68.63; H, 11.12; N, 2.26; P, 1.66.

EXAMPLE 25 (B24)

Preparation of *N*-[(*R*)-3-Tetradecanoyloxytetradecanoyl]-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=$CONH_2$, R_8=PO_3H_2).

(1) A suspension of L-serinamide hydrochloride (0.157 g, 1.18 mmol) and (*R*)-3-tetradecanoyloxytetradecanoic acid (0.61 g, 1.34 mmol) in CH_2Cl_2 (6 mL) was treated with triethylamine (0.18 mL, 1.3 mmol) and the resulting solution was stirred with 4Å molecular sieves for 30 min. EEDQ (0.437 g, 1.77 mmol) was then added and the mixture was stirred for 16 h at room temperature. The product that precipitated was collected and washed with CH_2Cl_2 (2 x 25 mL) to give 0.455 g (71%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-L-serinamide as a colorless powder: mp 126-130°C; ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, *J*= ~7 Hz), 1.15-1.7 (m, 42 H), 2.31 (t, 2 H, *J*=7.5 Hz), 2.51 (d, 2 H, *J*=6.3 Hz), 3.56 (br s, 1 H), 3.65 (dd, 1 H, *J*=11.2, 5.5 Hz), 3.86 (dd, 1 H, *J* =11.2, 4.5 Hz), 4.21 (s, 2 H), 4.40 (m, 1 H), 5.22 (m, 1 H).

(2) In the same manner as described in Example 2-(6), the compound prepared in (1) above (0.23 g, 0.246 mmol) and the compound prepared in Example 2-(4)

(0.961 g, 0.745 mmol) were coupled in the presence of mercury cyanide (0.43 g, 1.7 mmol) to give 0.527 g (71%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2,-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serinamide as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J*= ~7 H), 1.0-1.7 (m, 84 H), 1.80 and 1.89 (2s, 6 H), 2.21 (t, 2 H, *J*=7.5 Hz), 2.30 (t, 2 H, *J*=7.5 Hz), 2.37 (m, 2 H), 2.47 (m, 2 H), 3.54 (m, 1 H), 3.68 (dd, 1 H, *J*=8, *J*=11 Hz), 3.86 (br d, 1 H, *J*=11 Hz), 4.16 (dd, 1 H, *J*=11, 4 Hz), 4.24 (dd, 1 H, *J*=12, 4.3 Hz), 4.40 (d, 1 H, *J*=12 Hz), 4.6-4.8 (m, 4 H), 5.00 (d, 1 H, *J*=8 Hz), 5.1-5.25 (m, 2 H), 5.4-5.55 (m, 2 H), 5.84 (br s, 1 H), 6.61 (br s, 2 H), 7.1-7.35 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (0.44 g, 0.254 mmol) was deprotected with zinc (0.83 g, 13 mmol) and then acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.14 g, 0.31 mmol) in the presence of EEDQ (0.095 g, 0.38 mmol) to give 0.271 g (59%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 18 H, *J*=~6.5 Hz), 1.0-1.7 (m, 126 H), 2.03 (br s, 1 H), 2.15-2.55 (m, 12 H), 3.5-4.05 (m, 5 H), 4.14 (dd, 1 H, *J*=10, 3.5 Hz), 4.5-4.65 (m, 2 H), 4.68 (d, 1 H, *J*=8.1 Hz), 5.05-5.25 (m, 3 H), 5.31 (t, 1 H, *J*= ~10 Hz), 5.58 (br s, 1 H), 6.31 (d, 1 H, *J*=8 Hz), 6.85-6.95 (m, 2 H), 7.1-7.4 (m, 10 H).

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (0.25 g, 0.14 mmol) was hydrogenated in the presence of platinum oxide (0.125 g) to give 0.195 (80%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide triethylammonium salt as a colorless solid: mp 190-191 °C (dec); IR (film) 3418, 3293, 2921, 2850, 1732, 1717, 1651, 1636, 1557, 1540, 1458, 1165, 1033 cm^{-1}; ^{1}H NMR ($CDCl_3$—CD_3OD) δ 0.88 (t, 18 H, *J*= ~7 Hz), 1.0-1.7 (m, 135 H), 2.2-2.7 (m, 12 H), 3.05 (q, 6 H, *J*=7.2 Hz), 3.2-3.45 (m), 3.5-4.15 (m, 5 H), 4.21 (q, 1 H, *J*= ~10 Hz), 4.53 (d, 1 H, *J*=8.1 Hz), 4.58 (m, 1 H), 5.0-5.3 (m, 4 H), 7.25 (d, 1 H, *J*=8.4 Hz), 7.40 (d, 1 H, *J*=7.2 Hz); ^{13}C NMR

($CDCl_3$-CD_3OD) δ 173.7, 173.5, 172.5, 170.7, 170.5, 170.4, 101.4, 75.5, 73.4, 71.1, 70.9, 70.2, 68.6, 60.0, 53.9, 52.2, 45.6, 41.2, 41.0, 38.9, 34.4, 34.2, 31.8, 29.6, 29.5, 29.3, 29.1, 25.2, 24.9, 22.6, 14.0, 8.3.

Anal. Calcd for $C_{99}H_{191}N_4O_{18}P \cdot 2.5\ H_2O$: C, 66.00; H, 10.97; N, 3.11; P, 1.72. Found: C, 66.04; H, 10.99; N, 3.03; P, 1.95.

EXAMPLE 26 (B25)

Preparation of *N*-[(*R*)-3-Decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_9H_{19}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=$CONH_2$, R_8=PO_3H_2).

(1) In the same manner as described in Example 25-(1), L-serinamide hydrochloride (169 mg, 1.2 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (478 mg, 1.2 mmol) in the presence of EEDQ (371 mg, 1.5 mmol) in CH_2Cl_2 to afford 428 mg (74 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-L-serinamide as a white solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H), 1.1 - 1.7 (m, 34 H), 2.33 (t, 2 H, *J* = 7.5 Hz), 2.54 (d, 2 H, *J* = 6.6 Hz), 3.35 (s, 2 H), 3.72 (dd, 1 H, *J* = 11.0, 5.2 Hz), 3.84 (dd, 1 H, *J* = 11.3, 5.0 Hz), 4.20 (t, 1 H, *J* = 5.1 Hz), 5.26 (t, 1 H, *J* = 6.4 Hz).

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (410 mg, 0.85 mmol) and the compound prepared in Example 15-(4) (1.05g, 0.87 mmol) were coupled in the presence of AgOTf (560 mg, 2.2 mmol) to afford 780 g (56 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenyl phosphono-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serinamide as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H), 1.1 - 1.6 (m, 68 H), 1.80 (s, 3 H), 1.89 (s, 3 H), 2.30 (m, 8 H), 3.53 (m, 1 H), 3.68 (m, 1 H), 3.85 (br. d, 1 H, *J* = 9.4 Hz), 4.15 (dd, 1 H, *J* = 10.8, 3.7 Hz), 4.24 (dd, 1 H, *J* = 12.3, 4.6 Hz), 4.40 (d, 1 H, *J* = 10.8), 4.65 (m, 4 H), 5.00 (d, 1 H, *J* = 8.2 Hz), 5.18 (m, 2 H), 5.46 (m, 2 H), 5.83 (m, 1 H), 6.60 (m, 2 H), 7.30 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (600 mg, 0.36 mmol) was deprotected with zinc (1.19 g, 18.2 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (160 mg, 0.4 mmol) in the

presence of EEDQ (124 mg, 0.50 mmol) to afford 371 mg (62 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (330 mg, 0.20 mmol) was hydrogenated in the presence of platinum oxide (200 mg) to afford 120 mg (44 %) of *N*-[(*R*)-3-decanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-decanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serinamide triethylammonium salt as a white powder: mp 187-189° C; IR (film) 3419, 3286, 3220, 3098, 2955, 2922, 2852, 1732, 1680, 1662, 1644, 1559, 1467, 1247, 1167, 1107, 1080, 1051, 965, 913 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.89 (t, 18 H, *J* = 7.0 Hz), 1.1 - 1.7 (m, 111 H), 2.2 - 2.7 (m, 12 H), 3.07 (q, 6 H, *J* = 7.1 Hz), 3.68 (m, 1 H), 3.87 (m, 1 H), 4.09 (dd, 1 H, *J* = 10.8, 3.6 Hz), 4.22 (m, 1 H), 4.53 (d, 1 H, *J* = 8.2 Hz), 4.58 (m, 1 H), 5.13 (m, 3 H), 5.28 (m, 1 H), 7.53 (d, 1 H, *J* = 9.0 Hz), 7.56 (d, 1 H, *J* = 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 173.5, 173.2, 170.2, 169.8, 102.3, 75.7, 73.5, 71.3, 70.7, 70.1, 68.8, 60.8, 53.9, 51.7, 45.8, 41.5, 41.1, 39.1, 34.6, 34.5, 34.2, 32.0, 29.7, 29.6, 29.5, 29.4, 25.7, 25.4, 25.1, 22.7, 14.1, 8.6.

Anal. Calcd. for $C_{87}H_{167}N_4O_{18}P \cdot H_2O$: C, 65.05; H, 10.60; N, 3.49; P, 1.93. Found: C, 65.06; H, 10.40; N, 3.31; P, 2.00.

EXAMPLE 27 (B26)

Preparation of *N*-[(*R*)-3-Tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine Methyl Ester Triethylammoniun Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=p=q=0, R_4=R_5=R_7=R_9=H, R_6=CO_2Me, R_8=PO_3H_2).

(1) A solution of the compound prepared in Example 12-(2) (0.290 g, 0.157 mmol) in THF (20 mL) was hydrogenated in the presence of 5% palladium on carbon (50 mg) at room temperature and atmospheric pressure for 3 h. The catalyst was removed by filtration and the filtrate concentrated. A solution of the residue in $CHCl_3$ (5 mL) at 0°C was treated with a solution of diazomethane (0.5 mmol) in ether (5 mL) and then stirred for 30 min at 0°C. AcOH (0.5 mL) was added and the resulting colorless

solution was diluted with ether (50 mL), washed with saturated aqueous $NaHCO_3$ (25 mL), dried (Na_2SO_4) and concentrated. Flash chromatography on silica gel (gradient elution, 20 → 25% EtOAcs-hexanes) afforded 0.199 g (72%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichoro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine methyl ester as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, *J*= ~6.5 Hz), 1.1-1.75 (m, 84 H), 1.81 and 1.89 (2s, 6 H), 2.36 (t, 2 H, *J*=7.5 Hz), 2.25-2.6 (m, 6 H), 3.48 (q, 1 H, *J*= ~8 Hz), 3.7-3.9 (m, 5 H), 4.2-4.4 (m, 3 H), 4.6-4.85 (m, 4 H), 4.88 (d, 1 H, *J*=7.8 Hz), 5.03-5.22 (m, 2 H), 5.49 (t, 1 H, *J*= ~9.5 Hz), 6.21 (br s, 1 H), 6.59 (d, 1 H, *J*=7.8 Hz), 7.1-7.4 (m, 10 H).

(2) In the same manner as described in Example 2-(7), the compound prepared in (1) above (0.195 g, 0.111 mmol) was deprotected with zinc (0.36 g, 5.5 mmol) and acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.060 g, 0.13 mmol) in the presence of EEDQ (0.041 g, 0.17 mmol) to give 0.138 g (69%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[(*R*)-4-*O*-diphenylphosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl-β-D-glucopyranosyl]-L-serine methyl ester as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 18 H, *J*= ~6.5 Hz), 1.0-1.75 (m, 126 H), 2.15-2.45 (m, 10 H), 2.52 (dd, 1 H, *J*=14.7, 6 Hz), 2.66 (dd, 1 H, *J*=14.7, 6 Hz), 3.35 (br s, 1 H), 3.4-3.8 (m, 7 H), 3.88 (dd, 1 H, *J* =11 Hz), 4.18 (dd, 1 H, *J*=11 Hz), 4.6-4.75 (m, 2 H), 5.03 (d, 1 H, *J*=7.8 Hz), 5.1-5.25 (m, 3 H), 5.50 (t, 1 H, *J*= ~9.5 Hz), 6.50 (d, 1 H, *J*=7.2 Hz), 6.97 (d, 1 H, *J*=7.8 Hz), 7.1-7.4 (m, 10 H).

(3) In the same manner as described in Example 2-(8), the compound prepared in (2) above (0.100 g, 0.055 mmol) was hydrogenated in the presence of platinum oxide (50 mg) to give 0.055 g (57%) of *N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-*O*-[2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranosyl]-L-serine methyl ester triethylammonium salt as a colorless solid: mp 142-143°C (dec); IR (film) 3289, 2955, 2921, 2852, 1733, 1718, 1699, 1652, 1558, 1540, 1521, 1506, 1469, 1457, 1375, 1360, 1259 cm^{-1}; ^{1}H NMR ($CDCl_3$-CD_3OD) δ 0.88 (t, 18

H, J= ~6.5 Hz), 1.0-1.7 (m, 135 H), 2.2-2.7 (m, 12 H), 3.05 (q, 6 H, J=7.5 Hz), 3.31 (d, 1 H, J=9.3 Hz), 3.37 (s, 1 H), 3.55-3.9 (m, 10 H), 3.97 (d, 1 H, J=12 Hz), 4.1-4.25 (m, 2 H), 4.55-4.65 (m, 2 H), 5.05-5.25 (m, 3 H), 7.23 (d, 1 H, J=8.1 Hz), 7.47 (d, 1 H, J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 173.6, 173.4, 170.5, 170.4, 170.1, 100.7, 75.9, 72.8, 71.2, 70.8, 70.6, 68.5, 60.3, 55.3, 52.7, 52.4, 47.7, 41.5, 40.9, 39.7, 34.6, 34.5, 34.3, 32.0, 29.8, 29.4, 25.4, 25.1, 22.7, 14.2, 8.5.

Anal. Calcd for $C_{100}H_{192}N_3O_{19}P \cdot H_2O$: C, 67.11; H, 10.93; N, 2.35; P, 1.73. Found: C, 66.91; H, 10.93; N, 2.31; P, 2.11.

EXAMPLE 28 (B27)

Preparation of *N*-(Carboxymethyl)-*N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-aminoethyl 2-Deoxy-4-*O*-phophono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3=*n*-$C_{13}H_{27}CO$, X=Y=O, n=m=p=0, R_4=R_5=R_6=R_9=H, R_7=CO_2H, q=1, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), *N*-(2-hydroxyethyl)glycine *t*-butyl ester (0.25 g, 1.43 mmol) was acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.714 g, 1.57 mmol) in the presence of EDC·MeI (0.466 g, 1.57 mmol) to give 0.46 g (51%) of *N*-(2-hydroxyethyl)-*N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]glycine *t*-butyl ester as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6 H, J =~ 6.5 Hz), 1.15-1.7 (m, 51 H), 2.26 (t, 2 H, J = 7.5 Hz), 2.60 (dd, 1 H, J = 6.5, 15 Hz), 2.86 (dd, 1 H, J = 6.7, 15 Hz), 3.40-4.15 (m, 7 H), 5.25 (m, 1 H).

(2) In the same mannner as described in 13-(5), the compound prepared in (1) above (0.21 g, 0.334 mmol) and the compound prepared in Example 22-(2) (0.458g, 0.368 mmol) were coupled in the presence of AgOTf (0.688 g, 2.68 mmol) to give 0.39 g (64%) of *N*-(*t*-butyloxycarbonylmethyl)-*N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-aminoethyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside as an amorphous solid: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12 H, J =~ 6.5 Hz), 1.0-1.95 (m, 99 H), 2.1-2.6 (m, 7 H), 2.84 (dd, 1 H, J = 5, 15 Hz), 3.2-4.15 (m, 8

H), 4.15-4.45 (m, 2 H), 4.55-4.9 (m, 3 H), 5.00 (d, 1 H, J = 8 Hz), 5.13 (m, 2 H), 5.4-5.65 (m, 1 H), 6.16 (d, 1 H, J = 7 Hz), 7.05-7.4 (m, 10 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (0.339g, 0.185 mmol) was deprotected with zinc (0.36 g, 5.54 mmol) and then acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (0.100 g, 0.221 mmol) in the presence of EEDQ (0.068 g, 0.276 mmol) to give 0.25 g (71%) of *N*-(*t*-butyloxycarbonylmethyl)-*N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-aminoethyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside as a colorless solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (0.25 g, 0.131 mmol) was hydrogenated in the presence of platinum oxide (125 mg) in 9:1 THF-AcOH (15 mL). The crude hydrogenolysis product was dissolved in CH_2Cl_2 (1 mL), cooled to O°C, and treated dropwise with TFA (0.5 mL). After stirring for 2 h at O°C, the reaction mixture was concentrated and residual TFA was removed by azeotroping with toluene. The resulting residue (0.23 g) was dissolved in 1% aqueous triethylamine (12 mL) and lyophilized. Flash chromatography on silica gel with chloroform-methanol-water-triethylamine (91:8:0.5:0.5→85:15:0.5:0.5, gradient elution) and further purification by means of acidic extraction as described in Example 2-(8) and lyophilization from 1% aqueous triethylamine (6 mL) afforded 99 mg (43%) of *N*-(carboxymethyl)-*N*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-aminoethyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as colorless solid: mp 162-163°C (dec); IR (film) 3286, 2922, 2852, 1732, 1651, 1556, 1455, 1434, 1378, 1260, 1088, 801 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, 18 H, J =~ 6.5 Hz), 1.0-1.75 (m, 135 H), 2.2-3.0 (m, 14 H), 3.04 (q, 6 H, J = 7.2 Hz), 3.25-3.8 (m, 5 H), 3.85-4.3 (m, 5 H), 4.55 (d, 1 H, J = 7.5 Hz), 4.68 (d, 1 H, J = 8.1 Hz), 5.05-5.35 (m, 4 H).

Anal. Calcd for $C_{100}H_{192}N_3O_{19}P \cdot 3\ H_2O$: C, 65.79; H, 10.60; N, 2.30; P, 1.70. Found: C, 65.82; H, 10.44; N, 2.40; P, 1.79.

EXAMPLE 29 (B28)

Preparation of *N*-Carboxymethyl-*N*-[(*R*)-3-decanoyloxytetradecanoyl]-3-aminopropyl 2-Deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino])-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-β-D-glucopyranoside Triethylammonium Salt (Compound (I), R_1=R_2=R_3= *n*-$C_9H_{19}CO$, X=Y=O, n=1, m=p=0, R_4=R_5=R_6=R_9=H, R_7=CO_2H, q=1, R_8=PO_3H_2).

(1) In the same manner as described in Example 2-(5), *N*-(3-hydroxypropyl)glycine benzyl ester (450 mg, 2.0 mmol) was acylated with (*R*)-3-decanoyloxytetradecanoic acid (1.0 g, 2.5 mmol) in the presence of EDC·MeI (900 mg, 3.0 mmol) in CH_2Cl_2 to afford 0.76 g (63 %) of *N*-(3-hydroxypropyl)-*N*-[(*R*)-3-decanoyloxytetradecanoyl]glycine benzyl ester as a colorless oil: ^{1}H NMR ($CDCl_3$) (1 : 1 mixture of rotomers) δ 0.88 (t, 6 H, *J* = 6.6 Hz), 1.1 - 1.7 (m, 35 H), 1.78 (m, 1 H), 2.26 (q, 2 H, *J* = 7.6 Hz), 2.37 and 2.54 (2 dd, 1 H, *J* = 14.9, 6.9 Hz), 2.60 and 2.89 (2 dd, 1 H, *J* = 14.8, 6.0 Hz), 3.51 (m, 4 H), 3.70 (m, 1 H), 3.95 - 4.25 (m, 2 H), 5.1 - 5.25 (m, 3 H), 7.35 (m, 5 H).

(2) In the same manner as described in Example 13-(5), the compound prepared in (1) above (500 mg, 0.83 mmol), and the compound prepared in Example 15-(4) (1.0g, 0.83 mmol) were coupled in the presence of AgOTf (1.07 g, 4.15 mmol) to afford 1.27 g (72 %) of *N*-(benzyloxycarbonylmethyl)-*N*-[(*R*)-3-decanoyloxytetradecanoyl]-3-aminopropyl 2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-6-*O*-(2,2,2-trichloro-1,1-dimethylethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside benzyl ester: ^{1}H NMR ($CDCl_3$) (2 : 1 mixture of rotomers) δ 0.88 (t, 12 H, *J* = 6.9 Hz), 1.1 - 1.7 (m, 69 H), 1.80 (s, 3 H), 1.88 (s, 3 H), 2.1 - 2.6 (m, 11 H), 2.81 (dd, 1 H, *J* = 14.8, 6.2 Hz), 3.37 (m, 1 H), 3.52 (m, 2 H), 3.76 (m, 1 H), 3.87 (m, 1 H), 4.05 (m, 2 H), 4.28 (m, 3 H), 4.62 (m, 3 H), 4.77 (m, 1 H), 4.93 (d, 1 H, *J* = 8.2 Hz), 5.15 (m, 4 H), 5.46 and 5.61 (2 t, 1 H, *J* = 9.5 Hz), 5.95 and 6.05 (2 d, 1 H, *J* = 7.5 Hz), 7.1 - 7.4 (m, 15 H).

(3) In the same manner as described in Example 2-(7), the compound prepared in (2) above (1.25 g, 0.71 mmol) was deprotected with zinc (2.31 g, 3.53 mmol) and acylated with (*R*)-3-decanoyloxytetradecanoic acid (353 mg, 0.89 mmol) in the presence of EEDQ (264 mg, 1.07 mmol) to afford 670 mg (54 %) of *N*-benzyloxycarbonylmethyl-*N*-[(*R*)-3-decanoyloxytetradecanoyl]-3-aminopropyl 2-

deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-2-[(*R*)-3-decanoyloxytetradecanoylamino])-β-D-glucopyranoside as an amorphous solid.

(4) In the same manner as described in Example 2-(8), the compound prepared in (3) above (670 mg, 0.38 mmol) was hydrogenated in the presence of palladium hydroxide on carbon (270 mg) and platinum oxide (200 mg) in EtOH / AcOH (10:1) to afford 240 mg (39 %) of *N*-carboxymethyl-*N*-[(*R*)-3-decanoyloxytetradecanoyl]-3-aminopropyl 2-deoxy-4-*O*-phosphono-2-[(*R*)-3-decanoyloxytetradecanoylamino])-3-*O*-[(*R*)-3-decanoyoxytetradecanoyl]-β-D-glucopyranoside triethylammonium salt as a white powder: mp 156 - 157° C; IR (film) 3284, 2929, 2853, 2729, 1732, 1655, 1628, 1551, 1466, 1378, 1314, 1164, 1108, 1047, 955, 844, 722 cm^{-1}; ^1H NMR ($CDCl_3$ - CD_3OD) δ 0.88 (t, 18 H, J = 6.9 Hz), 1.1 - 1.7 (m, 111 H), 2.27 (q, 6 H, J = 6.2 Hz), 2.35 - 2.80 (m, 9 H), 3.05 (q, 6 H, J = 7.2 Hz), 3.25 - 3.60 (m, 4 H), 3.75 - 4.10 (m, 4 H), 4.23 (m, 2 H), 4.47 (d, 1 H, J = 8.2 Hz), 4.61 (d, 1 H, J = 8.3 Hz), 5.05 - 5.25 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 173.0, 171.1, 170.6, 170.3, 169.6, 100.5, 74.5, 73.9, 71.4, 71.2, 70.7, 70.2, 67.0, 65.8, 60.7, 54.6, 54.3, 51.4, 49.2, 46.0, 45.4, 42.1, 41.2, 39.4, 38.0, 37.7, 34.5, 34.3, 34.2, 31.9, 29.8, 29.7, 29.6, 29.5, 29.2, 28.1, 25.4, 25.3, 25.1, 22.7, 14.1, 11.1, 8.6.

Anal. Calcd. for $C_{89}H_{170}N_3O_{19}P \cdot H_2O$: C, 65.37; H, 10.60; N, 2.57; P, 1.89. Found: C, 65.35; H, 10.42; N, 2.43; P, 2.05.

TEST EXAMPLE 1

Stimulation of Anti-tetanus Toxoid Antibody Production.

The AGPs of the subject invention enhanced antibody production to purified tetanus toxoid in a murine model. Ten mg of each AGP sample was added to 1 ml of an oil-lecithin mixture containing squalene oil plus 12% lecithin. The mixtures were heated in a 56 °C water bath and sonicated to achieve clear solutions. Fifty (50) µl of each solution was emulsified by vortexing in 2 ml of sterile, pre-warmed 0.1% Tween 80 saline containing 1.0 µg tetanus toxoid antigen/ml. Preparations were vortexed again just prior to administration to mice. Female C57BL/6 x DBA/2 F_1 mice (8 per group) were treated with 0.2 ml of the appropriate preparation distributed as a 0.1 ml

subcutaneous injection into each flank. The final mouse dosage of the tetanus toxoid and AGP compounds was 0.2 μg and 50 μg, respectively. Control mice received tetanus toxoid in vehicle (oil-Tween saline). All mice were treated on day 0 followed by a second immunization on day 21. Fourteen days following the second immunization mice were bled and sera were isolated by centrifugation.

Serum samples from each mouse were evaluated for anti-tetanus toxoid antibodies by enzyme immunoassay (EIA) analysis using tetanus toxoid coated microtiter plates. Anti-tetanus antibody titers were evaluated for IgM, total Ig, as well as, IgG_1, IgG_{2a} and IgG_{2b} isotypes. Each serum sample was diluted 2-fold for eleven dilutions starting with an initial serum dilution of 1:200. Results are shown in Tables 2-4.

Table 2.
Anti-tetanus toxoid antibody titers of treated mice.

Material	Total IgG		IgG_1		IgG_{2a}		IgG_{2b}		IgM	
	T/C*	Titer	T/C	Titer	T/C	Titer	T/C	Titer	T/C	Titer
B11	3.6	23,200	1.86	400,000	2.06	10,450	0.93	26,800	4.75	7,600
B2	3.84	24,800	2.16	464,000	4.28	21,700	1.57	45,200	4.50	7,200
B1	3.97	25,600	3.42	736,000	3.78	19,200	2.45	70,400	2.38	3,800
B25	8.93	57,600	2.68	576,000	1.67	8,500	3.28	94,400	2.0	3,200
B21	4.71	30,400	2.23	480,000	5.83	29,600	6.07	174,400	5.50	8,800
B15	18.85	121,600	4.17	896,000	6.80	34,500	2.79	80,256	4.0	6,400
Vehicle		6,450		215,000		5,075		28,750		1,600

*T/C Ratio=Experimental Test Titer ÷ Vehicle Control Titer.

Table 3.

Anti-tetanus toxoid antibody titers of treated mice.

Material	T/C*	IgM	T/C	IgG_{2a}	T/C	IgG_{2b}
B12	3.1	4800	139.4	2370	149	9840
B16	1.6	2560	66.8	1135	104	6880
B13	3.9	6080	220	3740	>208	>13,760
B11	3.3	5120	347	5900	127.3	8400
Vehicle	-	1760	-	25	-	98

*T/C Ratio= Experimental Test Titers ÷ Vehicle Control Titers

Table 4.
Anti-tetanus toxoid antibody titers of treated mice.

Material	Total Ig		IgM		IgG_1		IgG_{2a}		IgG_{2b}	
	T/C	Titer	T/C	Titer	T/C	Titer	T/C	Titer	T/C	Titer
B26	10.5	2,490	1.1	600	16.9	25,200	29.3	440	42.6	2,260
B15	144.5	34,400	2.7	1,520	118.3	176,000	259.3	3,890	603.8	32,000
B22	60.0	19,050	0.8	440	18.4	27,400	345.8	5,187	59.6	3,160
B28	228.6	54,500	3.7	2,080	92.5	137,600	664.7	9,970	519.2	27,520
Vehicle		238		560		1,488		15		53

*T/C Ratio=Experimental Test Titer ÷ Vehicle Control Titer.

Compounds of the subject invention showed a dose response when administered with tetanus toxoid. BFD1 (C57B1/6 X DBA/2) female mice (8 per group) were immunized with 0.2 ml of emulsions containing AGP + 0.2 μg of tetanus toxoid. A second immunization was administered 21 days post primary immunization. Each mouse was bled 21 days after the second injection. The results are shown in Tables 5 and 6.

Table 5.
Dose response of AGPs in mice immunized with tetanus toxoid.

Material	Total Ig		IgM		IgG_1		IgG_{2a}		IgG_{2b}	
	T/C Ratio*	Titer	T/C Ratio	Titer	T/C Ratio	Titer	T/C Ratio	Titer	T/C Ratio	Titer
B15 50 µg	3.3	7,000	13.4	37,600	4.1	26,300	150.0	11,225	3.2	2500
B15 25 µg	5.8	12,400	2.1	6,000	4.5	28,800	52.0	3900	7.0	5400
B15 10 µg	5.3	11,450	1.4	4,000	5.5	35,100	33.8	2538	9.9	7650
B27 50 µg	3.2	6,800	4.0	11,200	1.6	10,400	12.0	900	11.6	9,000
Vehicle		2150		2800		6350		75		775

* T/C Ratio = Experimental Test Titer ÷ Vehicle Control Titer.

Table 6.

Dose response of AGPs in mice immunized with tetanus toxoid.

Material	IgM		Total Ig		IgG_1		IgG_{2a}		IgG_{2b}	
	T/C*	Titer	T/C	Titer	T/C	Titer	T/C	Titer	T/C	Titer
B12 50 µg	5.43	869	368.55	47,543	141.22	259,429		nd	499.35	12,983
B12 25 µg	3.14	503	403.98	52,114	145.21	266,743	16.86	354	196.92	5,120
B12 10 µg	3.71	594	248.06	32,000	81.12	149,029	6.81	143	181.12	4,709
B12 5 µg	3.43	549	489.92	63,200	84.11	154,514	34.14	717	352.54	9,166
B12 1 µg	1.71	274	326.02	42,057	90.08	165,486	73.71	1,548	175.81	4,571
B15 50 µg	3.14	503	233.88	30,171	90.08	165,486	50.05	1,051	235.62	6,126
B15 25 µg	2.29	366	181.91	23,467	106.14	194,971	10.43	219	158.23	4,114
B15 10 µg	2.86	457	170.10	21,943	39.07	71,771	2.57	54	84.38	2,194
B15 5 µg	1.71	274	248.06	32,000	103.15	189,486	3.00	63	210.88	5,483
B15 1 µg	1.57	251	166.56	21,486	72.04	132,343	7.62	160	114.27	2,971
Vehicle		160		129		1837		21		26

*T/C=Experimental Test Titer ÷ Vehicle Control Titer.

nd-not done

TEST EXAMPLE 2
Stimulation of Antiovalbumin Antibody Production.

BDF1 female mice (8 per group) were immunized with 0.2 ml of emulsions containing 50 μg of the AGPs + 50 μg of ovalbumin. A second immunization was administered 21 days post primary. Each mouse was bled 14 days after the second injection. Antibody titers of immunized mice showing total IgG and IgM as well as titers for the subgroups of IgG including IgG_1, IgG_{2a} and IgG_{2b} are given in Table 7.

Table 7.
Adjuvant activity in BDF1 mice immunized with ovalbumin.

Material	Total Ig		IgM	
	T/C*	Titer	T/C	Titer
B11	0.7	150	1.3	250
B2	2.5	563	0.9	175
B1	0.5	119	0.8	150
B25	1.9	438	0.8	150
B21	0.5	113	1.3	250
B15	4.1	925	2.3	438
B27	0.6	138	1.6	300
Vehicle	-	225	-	188

* T/C Ratio = Experimental Test Titer ÷ Vehicle Control Titer

Table 7 continued.

Material	IgG1		IgG2a		IgG2b	
	T/C*	Titer	T/C	Titer	T/C	Titer
B11	1.6	2650	1.7	550	1.6	375
B2	5.0	8300	2.5	825	2.3	550
B1	0.5	763	0.2	56	0.8	188
B25	5.2	8500	0.5	163	5.0	1188
B21	0.6	1000	0.1	25	0.8	200
B15	0.6	950	0.3	113	16.7	3963
B27	0.8	1275	0.1	38	0.5	113
Vehicle	-	1650	-	325	-	238

* T/C Ratio = Experimental Test Titer ÷ Vehicle Control Titer

The AGP compounds of the subject invention when administered to a warm-blooded animal with the antigen ovalbumin stimulates the production of antibody to that antigen.

TEST EXAMPLE 3
Generation of a Protective Immune Response to Infectious Influenza.

Mice vaccinated with formalin-inactivated influenza and the AGP compounds of the subject invention mounted a protective immune response to an influenza challenge as well as produced antibody to that antigen. Animals were vaccinated with the antigen and AGP compounds in various carriers. The degree of protection was determined by challenging the mice with intranasal (IN) admininstration of approximately 10 LD_{50} infectious influenza A/HK/68. Mortality was assessed for 21 days following the challenge. The number of mice surviving the challenge dose is a direct assessment of the efficacy of the vaccine. For the experiments provided this data does not necessarily correlate with the amount of antibody produced.

1) Vaccines were formulated in 0.2% triethanolamine (TEoA)/water solution containing: 1 hemagglutinating unit (HAU) of formalin-inactivated influenza A/HK/68 (FI-Flu), and 50 μg of AGP except the vehicle control vaccines which contained no AGP. ICR mice (10/group) were vaccinated 1 time only. The vaccines were administered by subcutaneous (SQ) injection of 0.1 ml/site at 2 distinct sites near the inguinal lymph nodes for a total of 0.2 ml of vaccine/mouse. Mice (only 5 mice/group) were bled from the orbital plexus 14 days following the vaccination. Sera was harvested and frozen at -20°C until used for enzyme-linked immunosorbent assay (ELISA). All mice were challenged 30 days post vaccination by intranasal (IN) administration of approximately 10 LD_{50} infectious influenza A/HK/68. Mortality was assessed for 21 days following the challenge. Anti-influenza antibody titers obtained from vaccinations with TEoA formulations and corresponding survival rates of mice vaccinated with this formulation are shown in Table 8.

Table 8.

Anti-influenza antibody titers and survival rates of treated mice.

Material	Titer[-1] Total IgG	Percent Survival
Nonimmune	<100	0
Vehicle	<100	0
B9	6400	44
B10	1600	40
B7	200	33
B3	1600	33
B14	6400	44
B15	6400	50

2) Vaccines were formulated in 2% Squalene solution containing: 1 hemagglutinating unit (HAU) of formalin-inactivated influenza A/HK/68 (FI-Flu), and 25 μg of AGP except the saline and vehicle control vaccines which contained no AGP. BALB/c mice (10/group) were vaccinated 1 time only. The vaccines were administered by subcutaneous (SQ) injection of 0.1 ml/site at 2 distinct sites near the

inguinal lymph nodes for a total of 0.2 ml of vaccine/mouse. Mice (only 5 mice/group) were bled from the orbital plexus 14 days following the vaccination. Sera was harvested and frozen at -20°C until used for enzyme-linked immunosorbent assay (ELISA). All mice were challenged 35 days post vaccination by intranasal (IN) administration of approximately 10 LD_{50} infectious influenza A/HK/68. Mortality was assessed for 21 days following the challenge. Anti-influenza antibody titers obtained from vaccinations with the squalene formulations as well as corresponding survival rates of vaccinated animals are shown in Table 9.

Table 9.

Anti-influenza antibody titers and survival rates of treated mice.

	Titer[-1]				
Material	**Total IgG**	**IgG_1**	**IgG_{2a}**	**IgG_{2b}**	**Percent Survival**
Nonimmune	<100	<100	<100	<100	0
Saline	800	100	800	100	62.5
Vehicle	1600	1600	1600	1600	100
B25	3200	1600	6400	1600	100
B15	1600	3200	3200	400	100
B9	1600	1600	3200	800	87.5
B10	400	400	400	400	62.5
B3	3200	3200	6400	800	87.5
B6	800	800	400	1600	75
B14	3200	6400	3200	6400	87.5
B28	800	400	400	100	50

3) The antibody titers and survival rate of vaccinated mice were compared after a primary then a secondary vaccination. Vaccines were formulated in 0.2% TEoA/water solution containing: 1 hemagglutinating unit of formalin-inactivated influenza A/HK/68, 25 μg AGP, except the vehicle control vaccine which contained no AGP. ICR mice (20/group) were administered vaccines by subcutaneous injection of 0.1 ml/site at 2 distinct sites near the inguinal lymph nodes for a total of 0.2 ml of vaccine/mouse. Each group was split into 2 subgroups 35 days after the primary

vaccination. One of each subgroup was challenged at this time, the remaining subgroups received a secondary vaccination. Mice (only 5/subgroup) were bled from the orbital plexus 14 days following vaccination (primary or secondary). Sera was harvested and frozen at -20°C until used for ELISA. Mice were challenged 35 post primary, or secondary, vaccination by intranasal administration of approximately 10 LD_{50}, or 40 LD_{50}, infectious influenza A/HK/68, respectively. Mortality was assessed for 21 days following the challenge. Anti-influenza antibody titers and survival rates of mice post primary and post secondary vaccination are shown in Table 10. Antibody titers as well as survival rates of mice vaccinated a second time were higher.

Table 10.
Antibody titers and survival rates of treated mice.

	IgG Titer[1]		Percent Survival	
Material	**post 1°**	**post 2°**	**post 1°**	**post 2°**
Nonimmune	200	100	0	0
Vehicle	800	102,400	20	40
B9	6400	12,800	80	50
B10	1600	25,600	60	90
B7	3200	>102,400	60	60
B4	800	25,600	50	70
B3	3200	102,400	70	60
B5	1600	>102,400	60	90
B6	1600	102,400	80	70
B14	800	51,200	33	70

TEST EXAMPLE 4
The Effect of Fatty Acid Chain Length on Adjuvanticity.

The effect of the length of fatty acid chains R_1-R_3 on activity was tested. Vaccines were formulated in 0.2% TEoA/water solution containing: 1 hemagglutinating unit of formalin-inactivated influenza A/HK/68, and 25 μg of AGP, except the vehicle control vaccines which contained no AGP. ICR mice (10/group)

were vaccinated 1 time only. The vaccines were administered by subcutaneous injection of 0.1 ml/site at 2 distinct sites near the inguinal lymph nodes for a total of 0.2 ml of vaccine/mouse. Mice (only 5 mice/group) were bled from the orbital plexus 14 days following the vaccination. Sera was harvested and frozen at -20°C until used for ELISA. All mice were challenged 35 post vaccination by intranasal administration of approximately 10 LD_{50} infectious influenza A/HK/68. Mortality was assessed for 21 days following the challenge. The length of the fatty acid chain appears to mildly affect biological activity. Results are shown in Tables 11 and 12.

Table 11.
Antibody titers and survival rates of treated mice.

Material	Chain Length	Titer^{-1} Total IgG	IgG_1	IgG_{2a}	IgG_{2b}	Percent Survival
Nonimmune	---	200	100	100	800	0
Vehicle	---	200	100	100	200	11
B18	7	800	800	800	400	20
B17	8	6400	3200	3200	1600	40
B16	9	800	1600	100	800	40
B15	10	3200	200	3200	6400	70
B14	10	800	1600	100	400	30
B13	11	1600	800	400	800	50
B12	12	200	200	100	200	0
B11	14	1600	200	1600	400	30

Table 12.
Antibody titers and survival rates of treated mice.

Material	Chain Length	Titer[-1] Total IgG	IgG_1	IgG_{2a}	IgG_{2b}	Percent Survival
Nonimmune	---	100	100	50	800	0
Vehicle	---	100	200	50	100	30
B8	7	6400	3200	400	1600	80
B7	9	3200	3200	100	1600	70
B5	10	800	200	50	400	44
B4	11	3200	400	100	1600	60
B3	12	1600	1600	50	800	0
B1	14	12,800	6400	1600	15600	40

TEST EXAMPLE 5

The Effect of Variations in the Carbon Chain Length Between the Heteroatom X and the Aglycon Nitrogen Atom on Adjuvanticity.

The length of the carbon chain between X and the aglycon nitrogen atom was extended progressively by a single atom. The effect of lengthening the chain between these two components on adjuvanticity was explored. Vaccines were formulated in 0.2% TEoA/water solution containing: 1 hemagglutinating unit of formalin-inactivated influenza A/HK/68, and 25 μg of AGP, except the vehicle control vaccines which containcd no AGP. ICR mice (10/group) were vaccinated 1 time only. The vaccines were administered by subcutaneous injection of 0.1 ml/site at 2 distinct sites near the inguinal lymph nodes for a total of 0.2 ml of vaccine/mouse. Mice (only 5 mice/group) were bled from the orbital plexus 14 days following the vaccination. Sera was harvested and frozen at -20°C until used for ELISA. All mice were challenged 35 days post vaccination by intranasal administration of approximately 10 LD_{50} infectious influenza A/HK/68. Mortality was assessed for 21 days following the challenge. Adjuvant activity appears to lessen as the length of the carbon chain between the heteroatom X and aglycon nitrogen atom increases. However, depending upon the residues attached to this carbon chain the biologic and metabolic stability of the molecules may be affected. Results are shown in Tables 13.

Table 13.
Antibody titers and survival rates of treated mice.

Material	Carbon Chain	Titer[-1]				
		Total IgG	IgG_1	IgG_{2a}	IgG_{2b}	Percent Survival
Nonimmune	---	<50	<50	<50	<50	0
Vehicle	---	200	200	50	200	25
B19	2	12,800	100	800	6400	50
B21	3	6400	800	100	1600	40
B22	4	3200	100	3200	200	40

TEST EXAMPLE 6
Cytokine Induction by the AGP Compounds.

The AGP compounds of the subject invention induced cytokines in human whole blood *ex vivo* culture assays. AGP compounds were solubilized in 10% EtOH-water and diluted to various concentrations. Fifty µl of each dilution were added to 450 µl of whole human blood. Controls were treated with culture media (RPMI). The reaction mixture was incubated at 37°C for 4 hr with constant mixing on a rotator. Sterile PBS (1.5 ml) was added to the reaction mixture, the cells were centrifuged and the supernatents removed for cytokine testing. The concentration of TNF-α and IL-1β in each supernatent was determined using immunoassay ELISA kits from R&D Systems. Results from these studies are shown in Tables 14-19.

Table 14.
Stimulation of cytokine secretion in an *ex vivo* assay.

Material	**Dosage** (µg)	**TNF-α** (pg/ml)	**IL-1β** (pg/ml)
B26	20	498.90	33.25
	10	254.94	25.34
	5	75.62	9.89
	1	38.85	3.90
B2	20	1338.42	155.07
	10	817.67	114.41
	5	235.32	34.72
	1	105.52	14.53
RPMI	-	2	0

Table 15.
Stimulation of cytokines in an *ex vivo* assay.

Material	Dosage (ng/ml)	TNF-α (pg/ml)	IL-1β (pg/ml)
B16	10,000	291	55
	5000	277	53
	1000	155	39
B13	10,000	775	THTC*
	5000	716	187
	1000	740	177
B9	10,000	449	96
	5000	247	84
	1000	145	53
B10	10,000	207	43
	5000	127	61
	1000	73	17
B7	10,000	83	16
	5000	57	14
	1000	26	6
RPMI	-	2	0

*THTC-To high to Count

Table 16.
Stimulation of cytokines in an *ex vivo* assay.

Material	Dosage (ng/ml)	TNF-α (pg/ml)	IL-1β (pg/ml)
B4	10,000	432	213
	5000	205	164
	1000	94	70
B3	10,000	567	269
	5000	390	342
	1000	189	204
B5	10,000	169	79
	5000	143	162
	1000	43	36
B6	10,000	94	52
	5000	59	29
	1000	30	13
B14	10,000	249	91
	5000	120	71
	1000	56	46
RPMI	-	2	0

Table 17.
Stimulation of cytokine secretion in an *ex vivo* assay.

Material	**Dosage** (ng/ml)	**TNF-α** (pg/ml)	**IL-1β** (pg/ml)
B11	10,000	181	62.3
	5000	139	61.7
	1000	115	54.5
	500	125	55.8
	100	127	59.8
B13	10,000	583	282
	5000	592	390
	1000	478	327
	500	411	352
	100	302	261
B15	10,000	320	153
	5000	280	126
	1000	209	94.4
	500	183	104
	100	133	51.6
B16	10,000	121	41.0
	5000	114	34.0
	1000	72	19.5
	500	55	17.1
B14	10,000	114	24.6
	5000	87	19.0
	1000	51	10.0
	500	49	19.9
RPMI	-	2	0

Table 18.
Stimulation of cytokine secretion in an *ex vivo* assay.

Material	Dosage (ng/ml)	TNF-α (pg/ml)	IL-1β (pg/ml)
B2	10,000	100	22.2
	5000	75	14.0
	1000	38	9.0
	500	28	8.3
	100	6.1	3.5
B1	10,000	20	10.0
	5000	11	5.5
	1000	2.8	4.0
	500	1.1	0
	100	0	0
B7	10,000	61	14.7
	5000	44	8.3
	1000	30	4.3
	500	27	3.8
	100	10	5.1
B4	10,000	232	66.9
	5000	173	66.5
	1000	130	32.0
	500	116	19.3
	100	89	65.2
B3	10,000	433	151.9
	5000	316	200.4
	1000	229	75.1
	500	212	67.9
	100	130	35.9
B5	10,000	142	24.1
	5000	99	23.0
	1000	96	10.5
	500	59	16.9
	100	33	5.4
RPMI	-	2	0

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Table 19.
Stimulation of cytokine secretion in an *ex vivo* assay.

Material	Dosage (ng/ml)	TNF-α (pg/ml)	IL-1β (pg/ml)
B17	10,000	2.8	0
	5000	2.2	0
	1000	2.6	0.2
B8	10,000	2.8	0
	5000	0.7	0.5
	1000	1.5	0.1
B22	10,000	287	17
	5000	11	1.9
	1000	2.2	0.1
B28	10,000	198	13
	5000	197	13
	1000	139	8
B12	10,000	1017	135
	5000	957	153
	1000	863	175
RPMI	-	3.9	0

TEST EXAMPLE 7
Stimulation of a Cytotoxic T-lymphocyte Response.

The induction of a cytotoxic T-lymphocyte response after administration of the AGP compounds of the subject invention and a protein antigen was detected by a cytotoxicity assay. Groups of C57BL/6 mice were given a primary immunization subcutaneously (inguinal region) with 25 µg ovalbumin (OVA) formulated in AGP preparations. The injected volume was 200 µl. Twenty-one days later three mice per experimental group were killed and spleens removed and pooled as single cell suspensions and counted.

Spleen cells (75 X 10^6 cells in 3-4 ml media) from the experimental groups were placed in a 25 cm^2 T-flask. Next, 1.0 ml of irradiated (20,000 rads) E.G7 (OVA) cells at 5 X 10^6/ml were added to the flask. The volume was brought to 10 ml. The cultures were maintained by placing the T-flasks upright in a 37°C, 5% CO_2 incubator for four days. On day 4 the surviving cells were recovered from the flasks, washed 1X in fresh media resuspended in 5.0 ml, and counted.

Recovered effector cells were adjusted to 5 X 10^6 viable cells/ml and 100 µl volumes were diluted serially in triplicate in wells of 96 well round-bottom plates (Corning 25850) using 100 µl/well of media as a diluent. Next, 100 µl volumes of ^{51}Cr-labelled (see below) targets [E.G7 (OVA)-an ovalbumin gene transfected EL-4 cell line] at 1 X 10^5 cells/ml were added to the wells. Spontaneous release (SR) wells contained 100 µl of targets and 100 µl of media. Maximal release (MR) wells contained 100 µl of targets and 100 µl detergent (2% Tween 20). Effector/target (E/T) ratios were 50:1, 25:1, 12.5:1. The plates were centrifuged at 400 Xg and incubated at 37°C, 5% CO_2 for 4 hr. After the incubation the well supernatants were collected using a Skatron Supernatant Collection System.

Percent specific lysis=

$$100\ X\left[\frac{(Exp.Release\ -\ SR)}{(MR\ -\ SR)}\right]$$

Target cells, E.G7 (OVA), were labelled with ^{51}Cr (sodium chromate) as follows. In a total volume of 1.0 ml were mixed 5 X 10^6 target cells and 250 µCi ^{51}Cr

in 15 ml conical tube. The cell suspensions was incubated in a 37°C water bath for 90 min., with gentle mixing every 15 min. After incubation the labelled cells were washed 3X by centrifugation and decanting with 15 ml volumes of media. After the third centrifugation the cells were resuspended in 10 ml of fresh media and allowed to stand at room temperature for 30 min. and then centrifuged. The cells were finally resuspended in media at 1 X 10^5 cells/ml.

Mice immunized according to the procedure above with the AGPs of the subject invention displayed a cytotoxic T-lymphocyte response to the OVA antigen as shown in Table 20.

Table 20.

Cytotoxic T-lymphocyte response of treated cells.

	% Cytotoxicity		
	E:T		
Material	**50:1**	**25:1**	**12.5:1**
B11	14	8	5
B12	13	7	4
B13	28	15	10
B15	58	49	30
B16	42	29	20
B17	39	26	15
B18	36	20	15
B14	45	36	25
B28	28	15	9
B27	17	9	5

Table 20 continued.

	% Cytotoxicity		
	E:T		
Material	50:1	25:1	12.5:1
B1	34	24	15
B3	65	54	42
B4	72	66	60
B5	28	18	11
B7	57	44	29
B8	36	20	15
B10	65	56	38
B9	65	55	36
B6	54	41	37
B2	21	12	6
B25	65	55	43
B26	14	8	4
B22	58	42	31
B21	38	26	15
B19	59	42	33
B20	36	25	13
Vehicle Control	<10		

TEST EXAMPLE 8

Generation of Serum and Mucosal Antibody Titers to Tetanus-toxoid.

The AGPs of the subject invention elicited both a serum and mucosal immune response to purified tetanus toxoid when administered intranasally. Groups of BALB/c mice were given a primary immunization (1°) intranasally with 10 μg tetanus toxoid (TT) + 20 μg AGP formulated in an aqueous formulation (AF) in a

volume of 20 µl. A secondary immunization (2°) was given 14 days later and a tertiary immunization (3°) identical in composition to the first and second was administered 14 days later. Mice were bled on day 21 (day 7 post 2°) and day 38 (day 10 post 3°) and day 48 (day 20 post 3°). Vaginal wash/fecal extract samples were taken on day 7 post 2° and day 7 post 3°. Serum and wash samples were assayed for anti-TT antibody by standard ELISA methods. Results of these assays are shown in Tables 21 and 22 below.

The aqueous formulation comprises the AGPs of the subject invention and one or more surfactants. Surfactants useful in an aqueous composition include glycodeoxycholate, deoxycholate, sphingomyelin, sphingosine, phosphatidylcholine, 1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine, L-α-phosphatidylethanolamine, and 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine, or a mixture thereof. The aqueous formulation used in this example comprises the surfactant 1,2 dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) and was prepared as follows: briefly; a 4 mg/ml solution of DPPC was prepared in ethanol. An aliquot of the ethanol solution is added to the dried AGPs and swirled gently to wet the AGP. The ethanol is removed by blowing a stream of filtered nitrogen gently over the vial. Water for Injection is added and the suspension is sonicated 10 min. at 60°C until clear. The resulting aqueous formulation contains approximately 118 µg/ml DPPC, has particles of around 70nm and was filter sterilized.

Table 21.
Anti-tetanus toxoid antibody titers in treated mice.

	Anti-Tetanus Toxoid Titer[-1]							
	Vaginal Wash				Fecal Extract			
	IgG		IgA		IgG		IgA	
Material	2°	3°	2°	3°	2°	3°	2°	3°
B25	800	6400	6400	6400	50	200	3200	6400
B15	400	800	6400	6400	50	100	6400	12,800
B19	200	400	1600	3200	25	25	3200	6400
B4	1600	400	1600	6400	25	50	3200	12,800
B5	3200	800	3200	3200	50	100	3200	6400
B3	1600	1600	6400	6400	50	100	3200	6400
B22	400	800	800	3200	25	50	1600	6400
PBS	<25	<25	<25	<25	<25	<25	<25	<25
Normal Sera	<25	<25	<25	<25	<25	<25	<25	<25

Table 22.
Serum anti-tetanus toxoid antibody titers in treated animals.

Anti-Tetanus Toxoid Titer^{-1}
Serum Pools

Material	IgG_1			IgG_{2a}			IgA		
	d21	**d38**	**d48**	**d21**	**d38**	**d48**	**d21**	**d38**	**d48**
B25	1M*	8M	8M	512K	4M	4M	12,800	102,400	102,400
B15	2M	8M	8M	512K	1M	2M	12,800	51,200	25,600
B19	2M	4M	4M	64K#	256K	128K	6,400	25,600	12,800
B4	1M	8M	8M	1M	2M	2M	25,600	102,400	102,400
B5	2M	8M	8M	512K	2M	2M	25,600	102,400	102,400
B3	512K	4M	8M	512K	2M	2M	12,800	51,200	51,200
B22	1M	2M	4M	64K	256K	256K	6,400	25,600	25,600
PBS	1,000	16K	16K	1,000	1,000	1,000	200	200	200
Normal Sera	200	200	200	100	100	100	200	200	200

*M=10^6, #K=10^3

Intranasal administration of TT formulated in AGP-AF induced both an antigen specific humoral immune response (Table 22) and a mucosal immune response (Table 21) to that antigen.

TEST EXAMPLE 9
Stimulation of an Immune Response to Hepatitis B Surface Antigen by Intranasal Administration

Mice administered hepatitis B surface antigen (HBsAg) intranasally with the compounds of the subject invention produced serum IgG and IgA titers to that antigen. Secretory IgA was detected in vaginal washes and the induction of a cytotoxic T-lymphocyte response was detected by a cytotoxicity assay.

Groups of BALB/c mice were given a primary immunization (1°) intranasally with 2.5 μg HBsAg + 10 μg AGP-AF in a volume of 20 μl. AGP-AF was prepared as in TEST EXAMPLE 8. Twenty-one days later mice were given a secondary immunization (2°) of 7.5 μg HBSAG + 10 μg AGP-AF intranasally in 20 μl volume. A tertiary immunization (3°) identical in composition to the secondary immunization was administered 28 days after the secondary immunization. Assays were conducted to detect cytotoxic T-lymphocyte activity at 16 days post secondary immunization (d16 post 2°) and 8 days post tertiary immunization (d8 post 3°). Serum and mucosal antibody titers were assessed at 22 days post secondary immunization (d22 post 2°) and 21 days post tertiary immunization (d21 post 3°). Antibody assays were conducted by standard ELISA methods. Cytotoxicity assays were conducted as described in TEST EXAMPLE 7. Results from this experiment are shown in Tables 23-26.

Table 23.
Cytotoxic T-lymphocyte response of treated cells.

	% Cytotoxicity (d16, post 2°) E/T			
Material	**50:1**	**25:1**	**12.5:1**	**6.25:1**
B25	36	20	13	9
B15	13	5	4	4
B19	26	20	11	9
B4	28	17	9	7
B3	43	26	17	11
B5	43	30	20	11
B22	33	21	15	8
Vehicle	3	2	0	0
Normal Cells	3	3	0	0

Table 24.
Cytotoxic T-lymphocyte response of treated cells.

	% Cytotoxicity (d8, post 3°) E/T			
Material	**50:1**	**25:1**	**12.5:1**	**6.25:1**
B25	30	19	13	8
B15	56	42	25	16
B19	71	54	33	24
B4	23	15	9	5
B3	54	45	32	20
B5	44	30	19	12
B22	22	13	7	5
Vehicle	5	2	1	1
Normal Cells	7	5	3	3

Table 25.
Anti-hepatitis antibody titers in treated mice.

	Anti HBsAg Titer^{-1}*		
Material	**IgG_1**	**IgG_{2a}**	**IgA**
B25	256K#	500K	3,200
B15	256K	500K	6,400
B19	500K	64K	1,600
B4	500K	1000K	6,400
B3	1000K	500K	6,400
B5	256K	500K	3,200
B22	256K	64K	1,600
Vehicle	<2K	<2K	<200

* day 22 post 2°, #K=10^3

Table 26.
Anti-hepatitis antibody titers in treated mice.

	Anti HBsAg Titer^{-1}*		
Material	**IgG_1**	**IgG_{2a}**	**IgA**
B25	1000K#	1000K	25,600
B15	2000K	2000K	25,600
B19	2000K	500K	12,800
B4	1000K	2000K	25,600
B3	1000K	1000K	25,600
B5	500K	1000K	12,800
B22	500K	500K	12,800
Vehicle	<2K	<2K	<200

* day 21 post 3°, #K=10^3

Groups of BALB/c mice were immunized with 2.5 μg HBsAg + 10 μg AGP-AF intranasally and boosted intranasally with 7.5 μg HBsAg + 10 μg AGP-AF 21 days later. Vaginal samples were collected 10 days after the booster immunization and assayed for anti-HBsAg antibody. Results of this assay are shown in Table 27.

Table 27.

	Vaginal Wash Anti-HBsAg Titer^{-1}	
Material	**IgG**	**IgA**
B25	100	800
B15	50	3200
B19	<50	400
B4	1600	6400
B3	800	1600
B5	1600	1600
B22	100	800
Vehicle	<50	<50

The intranasal administration of HBsAg with the compounds of the subject invention stimulated both a humoral and cellular immune response to that antigen. Intranasal immunization with the antigen formulated in AGP-AF induced a cytotoxic T-lymphocyte response (Table 23-24) and antigen specific humoral (Table 25 and 26) and mucosal (Table 27) immune responses.

TEST EXAMPLE 10
Generation of a Protective Immune Response to Influenza

Mice immunized intranasally with FLUSHIELD influenza vaccine containing hemagglutinin antigen and the AGPs of the subject invention produced both IgG and IgA which were recovered in vaginal washes. Immunized mice were also protected from subsequent influenza challenge.

ICR mice were immunized three times at 21 day intervals intranasally with FLUSHIELD influenza vaccine (Wyeth-Lederle) containing 0.3 μg hemagglutinin antigen (HA) + 10 μg AGP-AF or recombinant *E. coli* heat labile enterotoxin (LT). AGP-AF was prepared as in TEST EXAMPLE 8. LT was solubilized in saline at 1 μg/ml. Vaginal washes were collected 14 days after the second and third

immunization. Serum samples were collected 14 days after the third immunization. Mice were challenged with 10 LD_{50} (lethal dose 50) of infectious influenza A/HK/68 thirty-five days after the final immunization and monitored for mortality. Tables 28 and 29 show the results of assays conducted by standard ELISA methods to detect anti-influenza antibody titers in vaginal washes and sera.

Table 28.

Material	Vaginal Wash Samples				Percent
	IgA		IgG		
	Secondary	Tertiary	Secondary	Tertiary	Protection
Nonimmune	<20	<20	<20	<20	22
Vehicle	80	160	160	160	50
B25	1280	1280	640	2560	100
B19	320	5120	1280	1280	70
B3	1280	2560	1280	1280	100
B22	640	2560	320	640	75
LT	2560	2560	2560	640	100

Table 29.

Material	Serum Titers				Percent
	Total IgG	IgG_1	IgG_{2a}	IgG_{2b}	Protection
Nonimmune	<400	<400	<400	<400	22
Vehicle	102,400	256,000	12,800	102,400	50
B25	≥819,200	102,400	819,200	≥819,200	100
B19	819,200	51,200	102,400	819,200	70
B3	≥819,200	51,200	819,200	≥819,200	100
B22	819,200	51,200	102,400	819,200	75
LT	≥819,200	≥819,200	≥819,200	≥819,200	100

These data demonstrate that AGPs in AF when administered intranasally act as a mucosal adjuvants causing the production of IgA at mucosal sites. Increased protection is also induced against an upper respiratory pathogen which invades through the mucosa.

TEST EXAMPLE 11

Generation of Immune Responses from Stable Emulsion Formulations.

The AGP compounds of the subject invention stimulated both humoral and cytotoxic T-lymphocyte responses when formulated in a stable emulsion (SE). AGPs were tested at 25 μg dose levels to adjuvantize Hepatitis B surfacc antigen (HBsAg) for the induction of CTL and antibody responses. BALB/c mice were immunized subcutaneously with 2.0 μg HBsAg plus 25 μg of AGP/SE on day 0 and day 21. The CTL assay was conducted as in TEST EXAMPLE 7. The AGPs were formulated in a stable emulsion (SE) and the compositions were designated AGP-SE. Methods for preparing the stable emulsion containing 10% v/v squalene, 0.091% w/v PLURONIC-F68 block copolymer, 1.909% w/v egg phosphatidyl choline, 1.8% v/v glycerol, 0.05% w/v α tocopherol, 10% ammonium phosphate buffer and 78.2% v/v Water for Injection should be readily apparent to one skilled in the art. The emulsion was homogenized to a particle size of ≤0.2 μm. Table 30 shows the AGPs of the subject invention induced a cytotoxic T-lymphocyte response to HBsAg.

Table 30.
Cytotoxic T-lymphocyte response of treated cells.

		% Cytotoxicity E:T			
Material	**Day**	**50:1**	**25:1**	**12.5:1**	**6.25:1**
B25	d17,post 1°	27	12	9	5
B19		74	48	34	24
B3		28	15	9	5
B22		42	24	17	7
Vehicle-SE		32	16	9	6
	d16, post 2°				
B25		49	28	20	13
B19		73	62	42	31
B3		81	47	32	22
B22		78	69	58	39
Vehicle-SE		38	23	14	8

The results of the antibody titer to HBsAg are shown on Table 31. Sera from bleeds taken on day 28 post 2° were titered on ELISA plates coated with either HBsAg or a 28 amino acid peptide (p72) which contains B-cell epitopes found in the S-antigen region, residues 110-137, of the HBsAg.

Table 31.
Anti-HBsAg titer of treated mice.

	Anti-HBsAg Titer[-1]			
	HBsAg		**p72-Peptide**	
Material	**IgG_1**	**IgG_{2a}**	**IgG_1**	**IgG_{2a}**
B25	2048 K*	2048 K	128 K	64 K
B19	1024 K	1024 K	64 K	128 K
B3	512 K	1024 K	16 K	128 K
B22	1024 K	1024 K	128 K	128 K
Vehicle-SE	1024 K	64 K	64 K	4 K

AGP-SE treated mice displayed both humoral (Table 31) and cytotoxic T-lymphocyte (Table 30) responses to the hepatitis B surface antigen. Of interest, AGP-SE treated mice in serum displayed a vigorous IgG_{2a} specific antibody titer detected by both antigens, whereas the vehicle-SE induced only a modest IgG_{2a} response.

It is understood that the foregoing examples are merely illustrative of the present invention. Certain modifications of the compositions and/or methods employed may be made and still achieve the objectives of the invention. Such modifications are contemplated as within the scope of the claimed invention.

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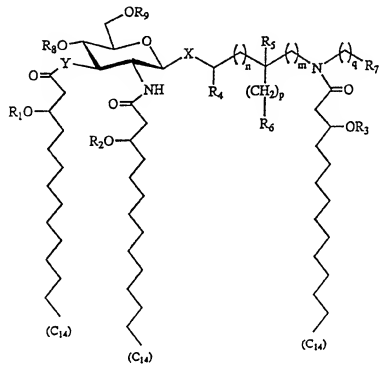
Claims

1. An immunoeffector compound having the following structure:



wherein, X is selected from the group consisting of O and S; Y is selected from the group consisting of O and NH; n, m, p and q are integers from 0 to 6; R_1, R_2 and R_3 are the same or different and are normal fatty acyl residues having from about 7 to about 16 carbon atoms; R_4 and R_5 are the same or different and are selected from the group consisting of H and methyl; R_6 and R_7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; and R_8 and R_9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R_8 and R_9 is phosphono.

2. The compound of claim 1, wherein R_6 is carboxy.

3. The compound of claim 2, wherein X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

4. The compound of claim 2, wherein X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

5. The compound of claim 2, wherein X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

6. The compound of claim 2, wherein X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 8 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

7. The compound of claim 1, wherein R_6 is H.

8. The compound of claim 7, wherein X is O; Y is O; n is 2; m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

9. The compound of claim 7, wherein X is O; Y is O; n is 1, m and p are 0; q is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_7 is carboxy; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

10. The compound of claim 7, wherein X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

11. The compound of claim 7, wherein X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

12. The compound of claim 7, wherein X is O; Y is O; m, p and q are 0; n is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbons; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

13. The compound of claim 1, wherein R_6 is hydroxy.

14. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; and R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

15. The compound of claim 13, wherein X is O; Y is O; m and q are 0; n and p are 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

16. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 2; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

17. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

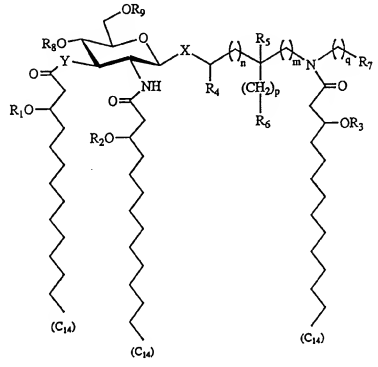
18. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

19. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 11 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

20. The compound of claim 13, wherein X is O; Y is O; m, n and q are 0; p is 1; R_4, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

21. The compound of claim 1, wherein X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_6 is amino carbonyl; R_7 is H; R_8 is phosphono; and R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

22. A method for enhancing the immune response of a mammal comprising administering to the mammal an effective amount of a compound having the following structure:



wherein, X is selected from the group consisting of O and S; Y is selected from the group consisting of O and NH; n, m, p and q are integers from 0 to 6; R_1, R_2 and R_3 are normal fatty acyl residues having from about 7 to about 16 carbon atoms; R_4 and R_5 are the same or different and are selected from the group consisting of H and methyl; R_6 and R_7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; R_8 and R_9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R_8 and R_9 is phosphono.

23. The method of claim 22, wherein R_6 of said compound is carboxy.

24. The method of claim 23, wherein said compound has the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

25. The method of claim 23, wherein said compound has the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

26. The method of claim 23, wherein said compound has the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

27. The method of claim 23, wherein said compound has the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 8 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

28. The method of claim 22, wherein R_6 of said compound is H.

29. The method of claim 28, wherein said compound has the following structure: X is O; Y is O; n is 2; m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

30. The method of claim 28, wherein said compound has the following structure: X is O; Y is O; n is 1, m and p are 0; q is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_7 is carboxy; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

31. The method of claim 28, wherein said compound has the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

32. The method of claim 28, wherein said compound has the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

33. The method of claim 28, wherein said compound has the following structure: X is O; Y is O; m, p and q are 0; n is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbons; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

34. The method of claim 22, wherein R_6 of said compound is hydroxy.

35. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; and R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_4 is attached to a stereogenic center having an *S* configuration.

36. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m and q are 0; n and p are 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

37. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 2; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

38. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

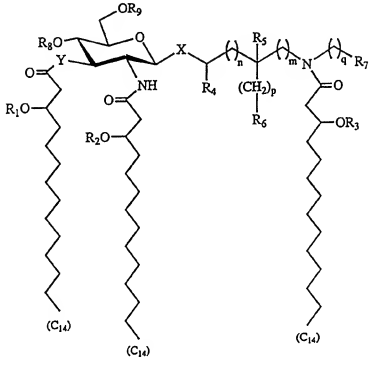
39. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

40. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 11 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

41. The method of claim 34, wherein said compound has the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_5 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

42. The method of claim 22, wherein said compound has the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms ; R_4 and R_5 are H; R_6 is amino carbonyl; R_7 is H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

43. A vaccine composition comprising a compound having the following structure:



wherein, X is selected from the group consisting of O and S; Y is selected from the group consisting of O and NH; n, m, p and q are integers from 0 to 6; R_1, R_2 and R_3 are the same or different and are normal fatty acyl residues having from about 7 to about 16 carbon atoms; R_4 and R_5 are the same or different and are selected from the group consisting of H and methyl; R_6 and R_7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; R_8 and R_9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R_8 and R_9 is phosphono, an antigen and a suitable carrier.

44. The composition of claim 43, wherein said composition comprises said compound where R_6 is carboxy.

45. The composition of claim 44, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

46. The composition of claim 44, whercin said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

47. The composition of claim 44, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

48. The composition of claim 44, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 8 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

49. The composition of claim 43, wherein said composition comprises said compound where R_6 is H.

50. The composition of claim 49, wherein said composition comprises said compound having the following structure: X is O; Y is O; n is 2; m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

51. The composition of claim 49, wherein said composition comprises said compound having the following structure: X is O; Y is O; n is 1, m and p are 0; q is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_7 is carboxy; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

52. The composition of claim 49, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

53. The composition of claim 49, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

54. The composition of claim 49, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, p and q are 0; n is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbons; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

55. The composition of claim 43, wherein composition comprises said compound where R_6 is hydroxy.

56. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; and R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

57. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m and q are 0; n and p are 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

58. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 2; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

59. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

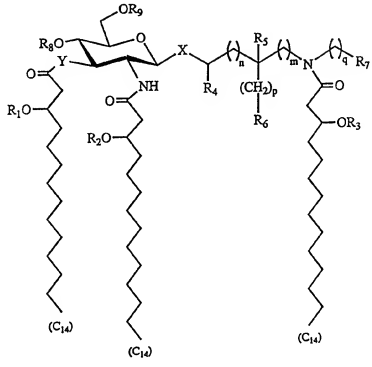
60. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

61. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 11 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

62. The composition of claim 55, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

63. The composition of claim 21, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_6 is amino carbonyl; R_7 is H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

64. A pharmaceutical composition comprising a compound having the following structure:



wherein, X is selected from the group consisting of O and S; Y is selected from the group consisting of O and NH; n, m, p and q are integers from 0 to 6; R_1, R_2 and R_3 are normal fatty acyl residues having from about 7 to about 16 carbon atoms; R_4 and R_5 are the same or different and are selected from the group consisting of H and methyl; R_6 and R_7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; R_8 and R_9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R_8 and R_9 is phosphono, and a pharmaceutically acceptable carrier.

65. The composition of claim 64, wherein said composition comprises said compound where R_6 is carboxy.

66. The composition of claim 65, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

67. The composition of claim 65, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

68. The composition of claim 65, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

69. The composition of claim 65, wherein said composition comprises said compound having the following structure: X is O; Y is O; n, m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 8 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

70. The composition of claim 64, wherein said composition comprises said compound where R_6 is H.

71. The composition of claim 70, wherein said composition comprises said compound having the following structure: X is O; Y is O; n is 2; m, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

72. The composition of claim 70, wherein said composition comprises said compound having the following structure: X is O; Y is O; n is 1, m and p are 0; q is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_7 is carboxy; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

73. The composition of claim 70, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5, and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

74. The composition of claim 70, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

75. The composition of claim 70, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, p and q are 0; n is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbons; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; and R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration.

76. The composition of claim 64, wherein said composition comprises said compound where R_6 is hydroxy.

77. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 12 carbon atoms; R_4 and R_5 are H; R_7 is H; R_8 is phosphono; and R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

78. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m and q are 0; n and p are 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

79. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 2; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

80. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *R* configuration.

81. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 14 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

82. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 11 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

83. The composition of claim 76, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n and q are 0; p is 1; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4, R_5 and R_7 are H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

84. The composition of claim 43, wherein said composition comprises said compound having the following structure: X is O; Y is O; m, n, p and q are 0; R_1, R_2 and R_3 are normal fatty acyl residues having 10 carbon atoms; R_4 and R_5 are H; R_6 is amino carbonyl; R_7 is H; R_8 is phosphono; R_9 is H; R_1, R_2 and R_3 are each attached to a stereogenic center having an *R* configuration; and R_5 is attached to a stereogenic center having an *S* configuration.

85. The composition of claim 64, wherein said pharmaceutically acceptable carrier is an aqueous composition comprising water and one or more surfactants selected from the group consisting of glycodeoxycholate, deoxycholate, sphingomyelin, sphingosine, phosphatidylcholine, 1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine, L-α-Phosphatidylethanolamine, and 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine, or a mixture thereof.

86. The composition of claim 85, wherein said one or more surfactant is 1,2-Dipalmitoyl-sn-glycero-3-phosphocholine.

87. The composition of claim 85, wherein the molar ratio of said compound to surfactant is from about 10:1 to about 10:5.

88. The composition of claim 85, wherein the molar ratio of said compound to surfactant is about 4:1.

89. The composition of claim 64, wherein said carrier is a stable emulsion comprising a metabolizable oil, one or more surfactants, an antioxidant and a component to make the emulsion isotonic.

90. The composition of claim 89, wherein said stable emulsion comprises 10% v/v squalene, 0.9% w/v PLURONIC-F68 block co-polymer, 1.9% w/v egg phosphatidyl choline, 1.75% v/v glycerol and 0.05% w/v α tocopherol.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 98/09385

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H15/04 A61K31/70

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07H A61K

Documentation searched other than minimumdocumentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	J.EUSTACHE ET AL.: "New Acyclic Analogues of Lipid A " CARBOHYDRATE RESEARCH, vol. 251, 1994, pages 251-267, XP002076487 see the whole document ---	1,21,43, 64
A	K.MIYAJIMA ET AL.: "Lipid A and Related Compounds. XXXI. Synthesis of Biologically Active N-Acylated L-Serine-Containing D-Glucosamine 4-Phosphate Derivatives of Lipid A." CHEMICAL AND PHARMACEUTICAL BULLETIN, vol. 44, no. 12, December 1996, pages 2268-2273, XP002076488 cited in the application see the whole document ---	1,21,43, 64
	-/--	

[X] Further documents are listed in the continuation of box C. [ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of theinternational search	Date of mailing of the international search report
4 September 1998	21/09/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx 31 651 epo nl, Fax: (+31-70) 340-3016	Scott, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interr al Application No
PCT/US 98/09385

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	„K.IKEDA ET AL.: "Synthesi of Biologically Active N-Acylated L-Serine-Containing Glucosamine-4-Phosphate Derivatives of Lipid A." CHEMICAL AND PHARMACEUTICAL BULLETIN, vol. 41, no. 10, October 1993, pages 1879-1881, XP002076489 cited in the application see the whole document -----	1,21,43, 64

1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 98/09385

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 21-42
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 21-42 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements tosuch an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invitepayment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No recurred additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.